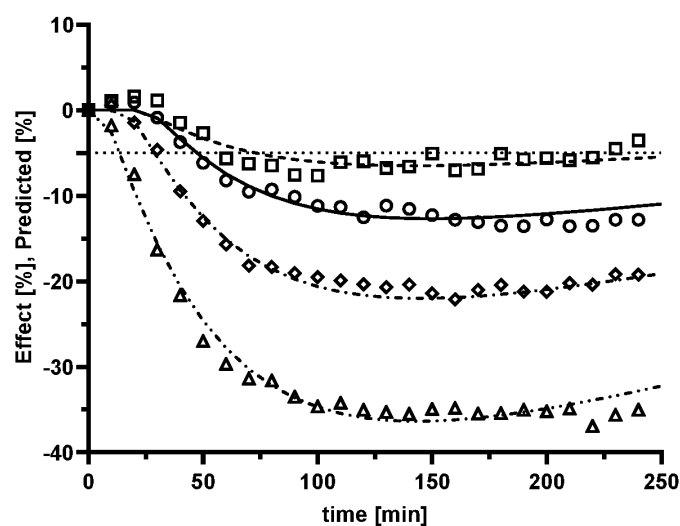


FIGURES

Observed		Predicted	
□	0.15µg/kg	---	0.15 µg/kg
○	0.5µg/kg	—	0.5 µg/kg
◇	1.5µg/kg	---	1.5 µg/kg
▲	5µg/kg	---	5 µg/kg

Fig. 1: Observed (symbols) and fitted (solid lines) pulmonary arterial pressure (=PAP) changes after administration of 0.15, 0.5, 1.5 and 5 µg/kg comparative example 11 (doses expressed as lung deposited doses) to minipigs (7 min inhalation as liquid aerosol). Relevant PAP reduction of 5% indicated as dotted line

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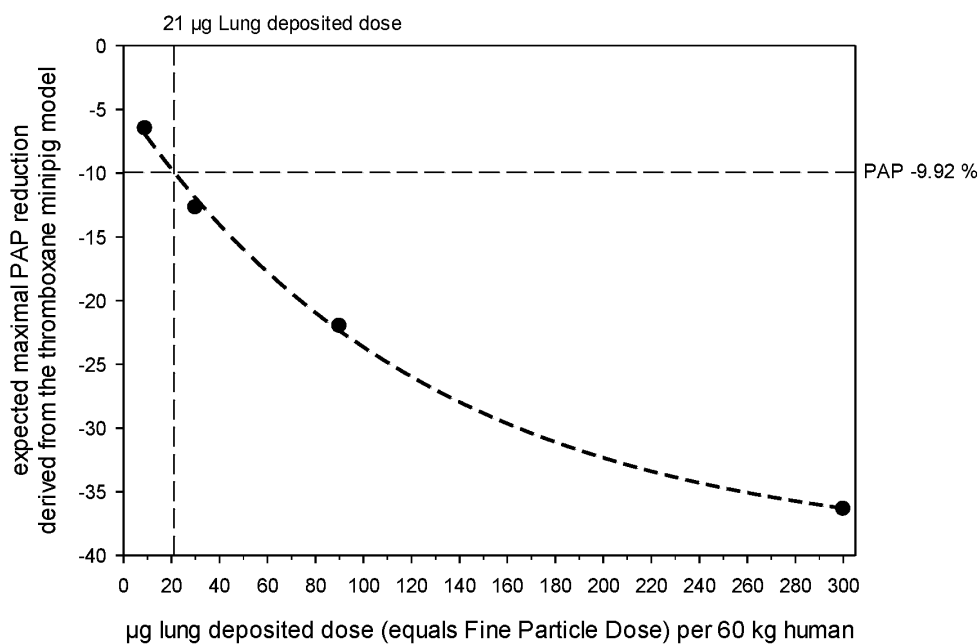


Fig. 2: Maximal expected PAP reduction for a 60 kg human at the corresponding lung deposited doses (FPD) based on the results of the anaesthetized thromboxane minipig model without considering interspecies differences in protein binding.

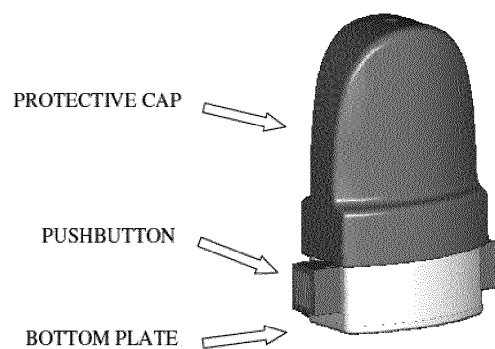


Fig. 3a: capsule based single-unit dose inhaler

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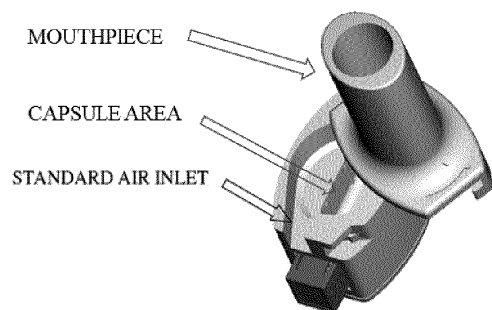


Fig. 3b: capsule based single-unit dose inhaler

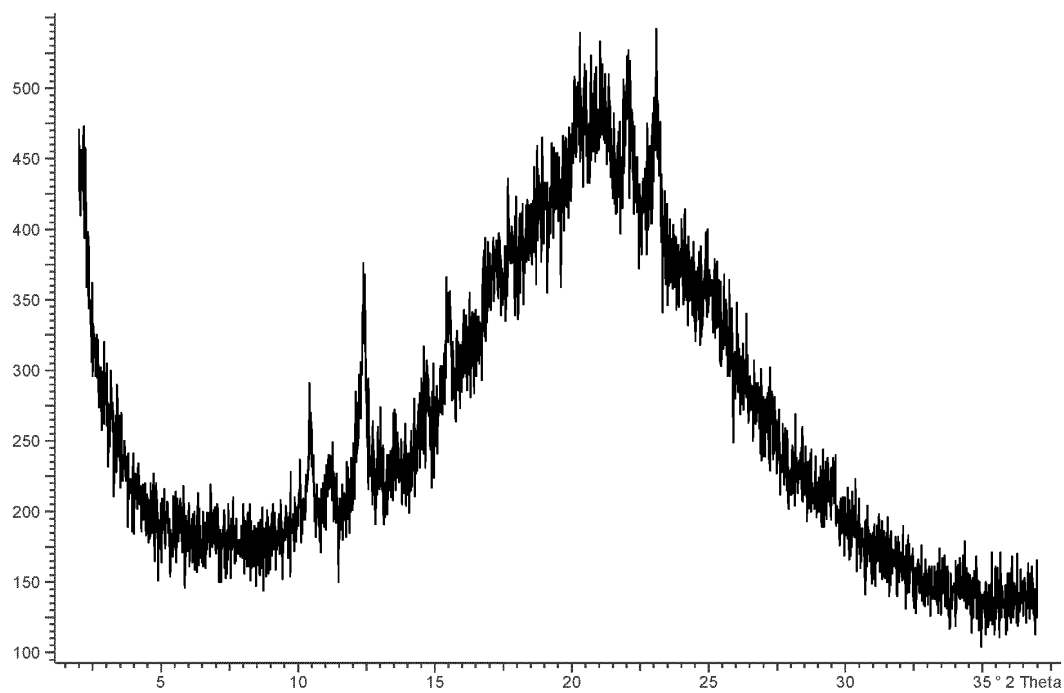


Fig. 4: X-Ray powder diffractogram of the amorphous residue build on salt screening experiments with L-arginine

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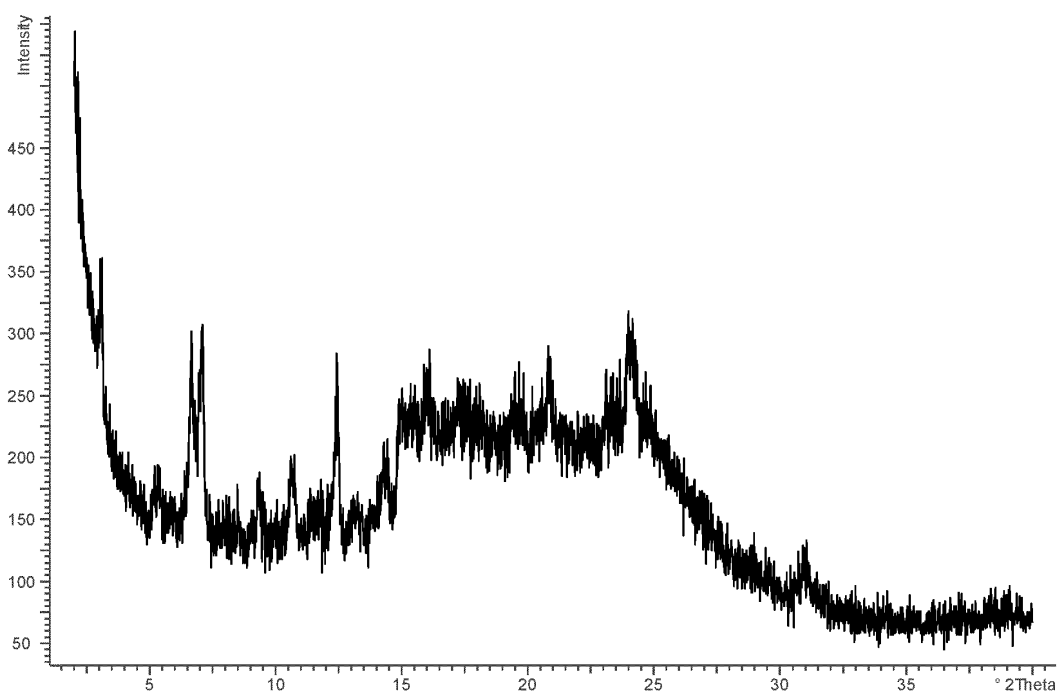


Fig. 5: X-Ray powder diffractogram of the Semihydrate, example 6a

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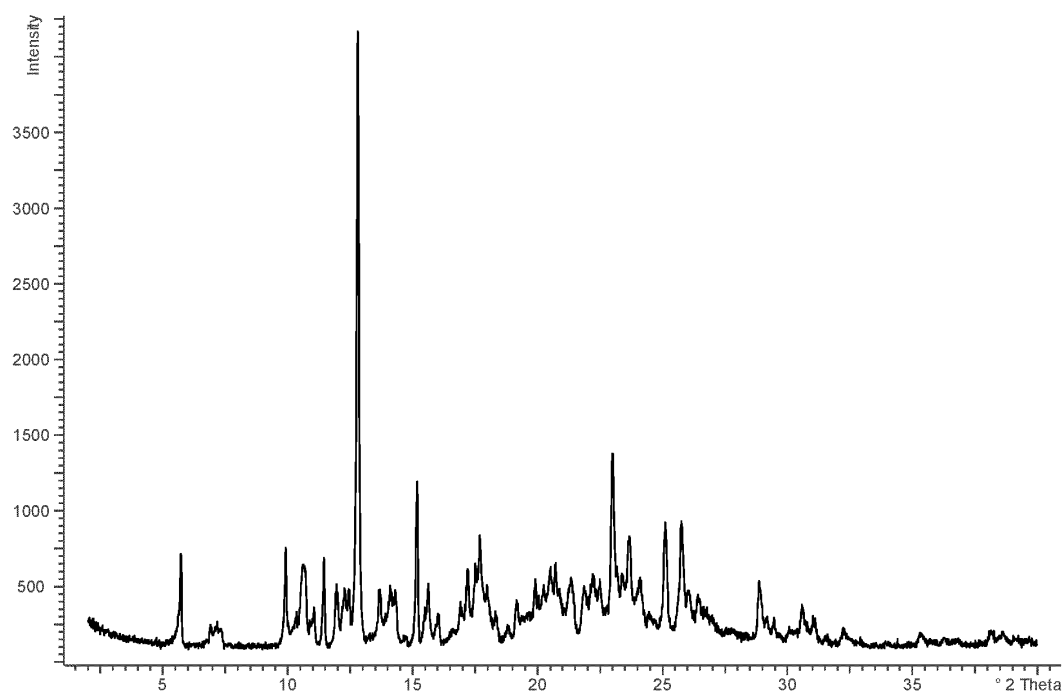


Fig. 6: X-Ray powder diffractogram of the Monohydrate I, example 6b

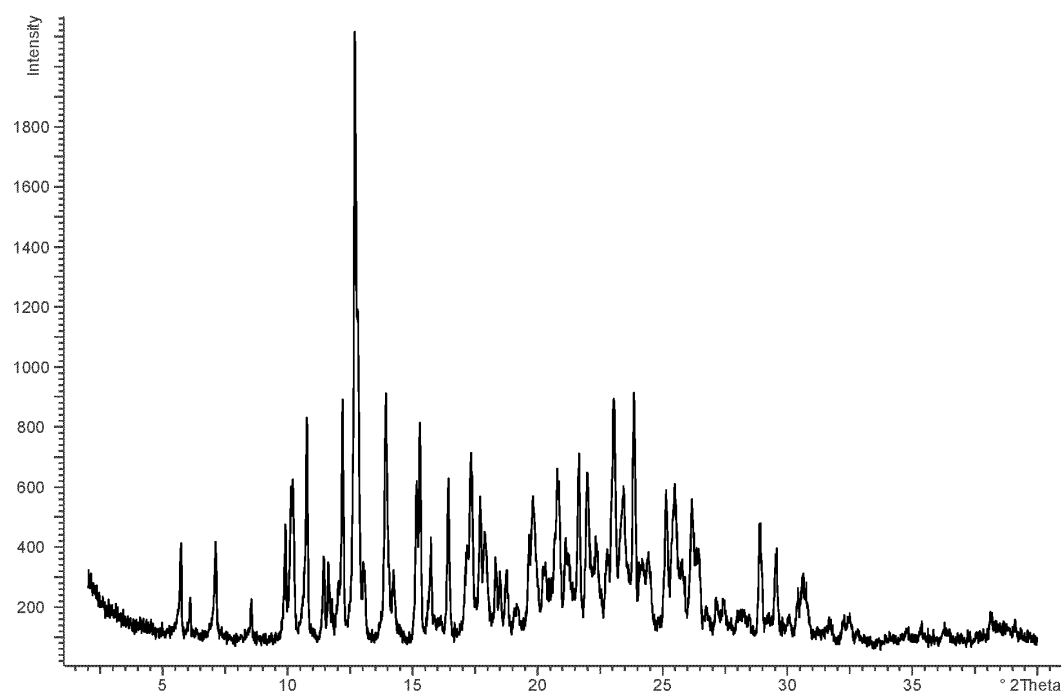


Fig. 7: X-Ray powder diffractogram of the Monohydrate II, example 6c

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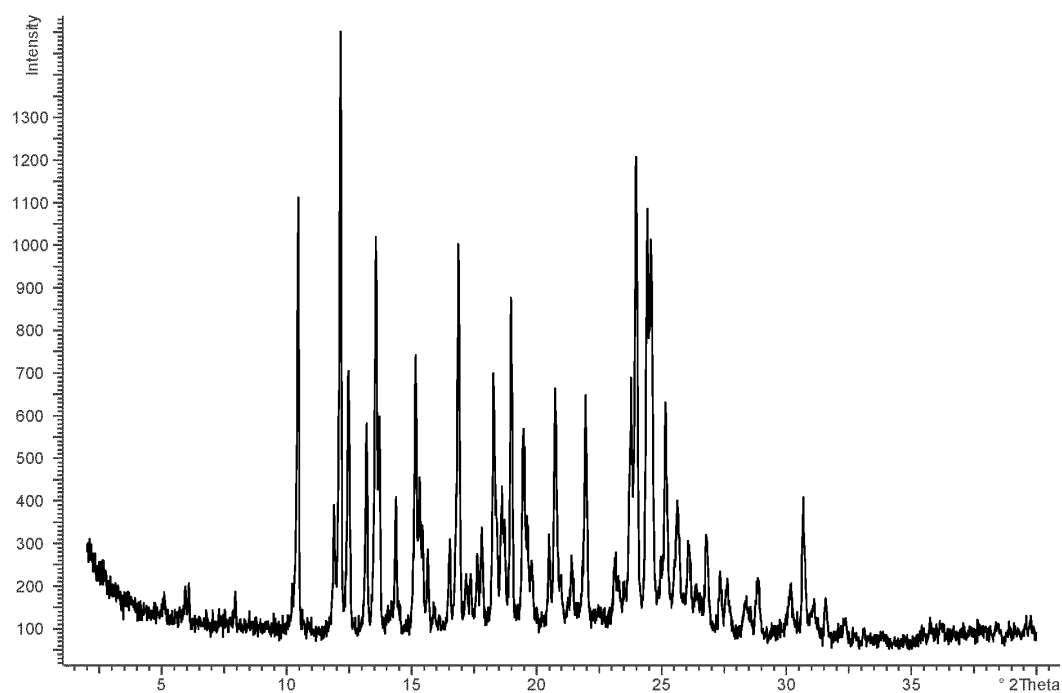


Fig. 8: X-Ray powder diffractogram of the 1,25-Hydrate, example 6d

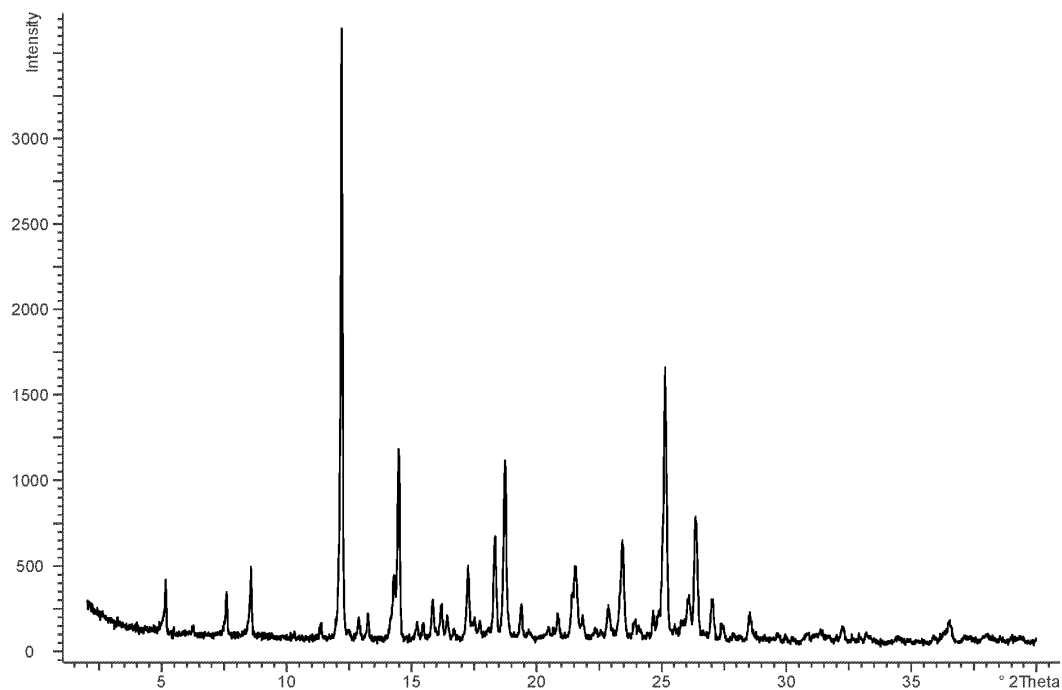
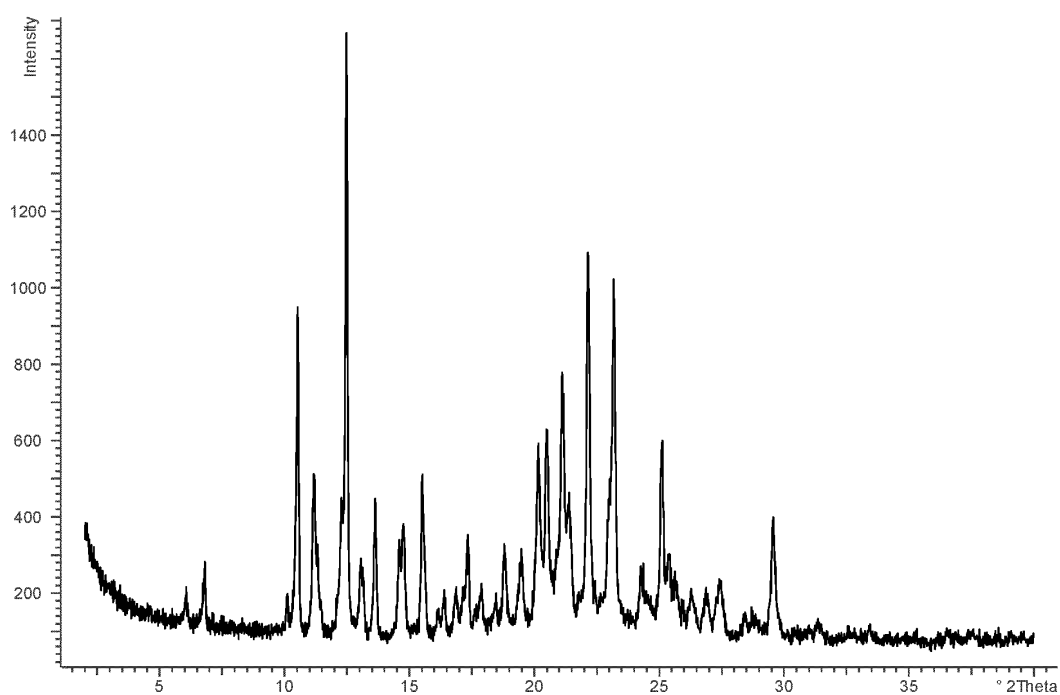
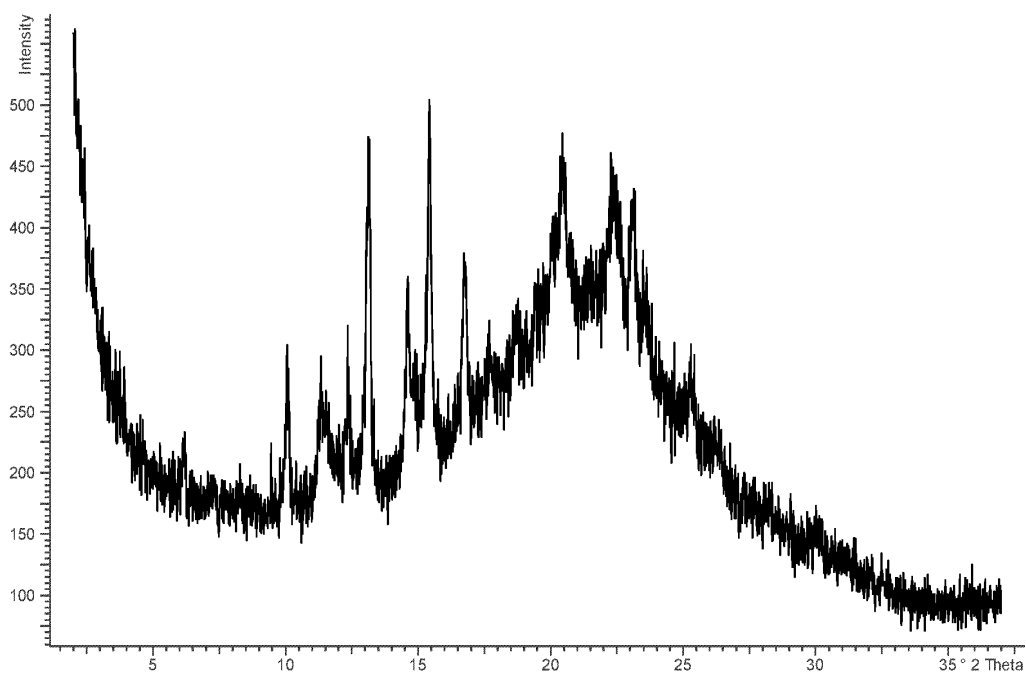


Fig. 9: X-Ray powder diffractogram of the Sesquihydrate, example 6e

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**Fig. 10:** X-Ray powder diffractogram of the Dihydrate, example 6f**Fig. 10a:** X-ray powder diffractogram of example 6f after drying

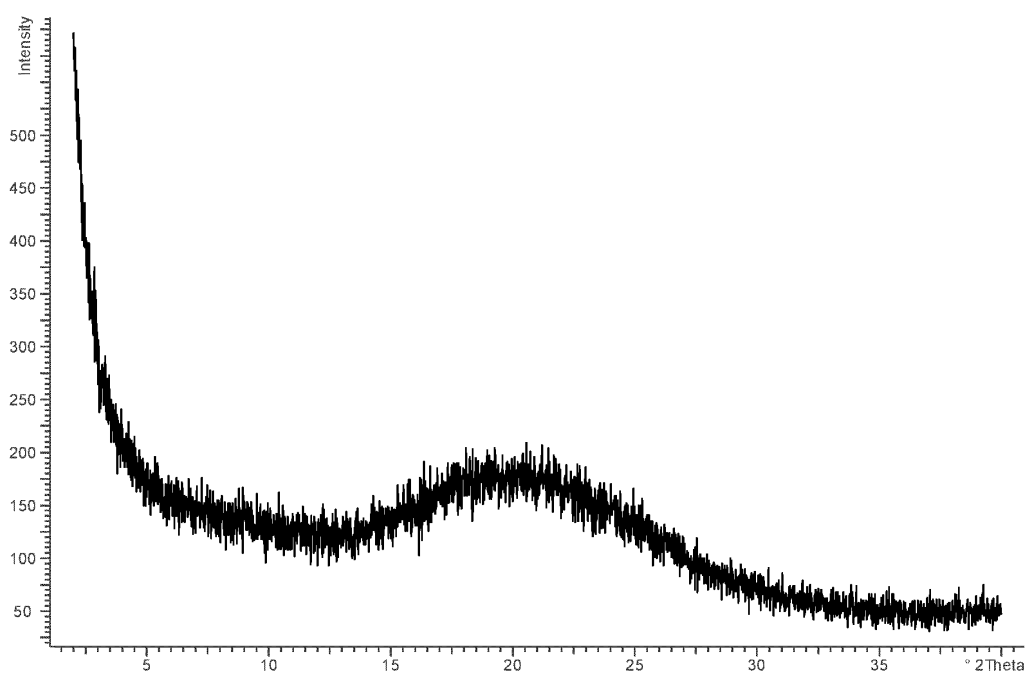


Fig. 11: X-Ray powder diffractogram of the amorphous form, example 6g

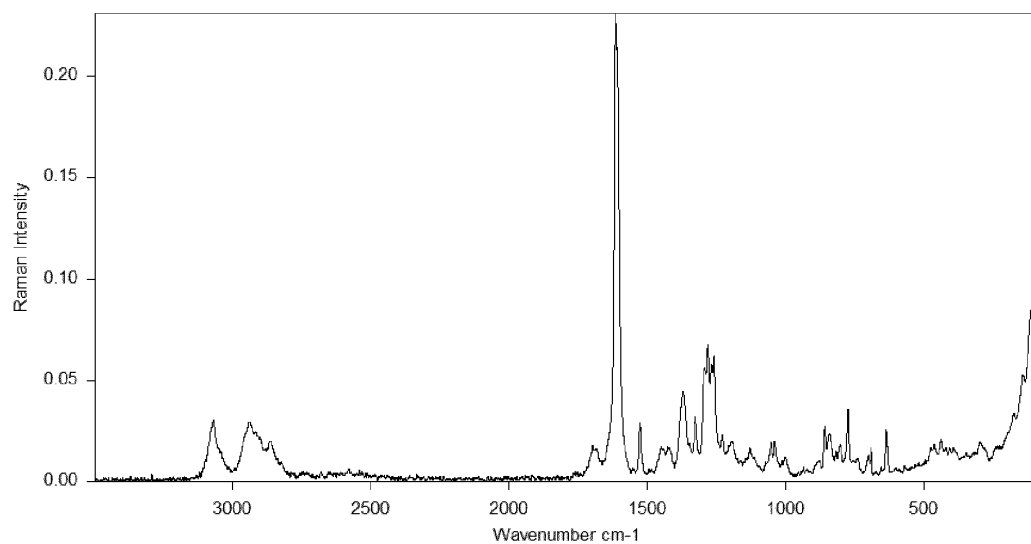


Fig. 12: Raman spectrum of the Semihydrate, example 6a

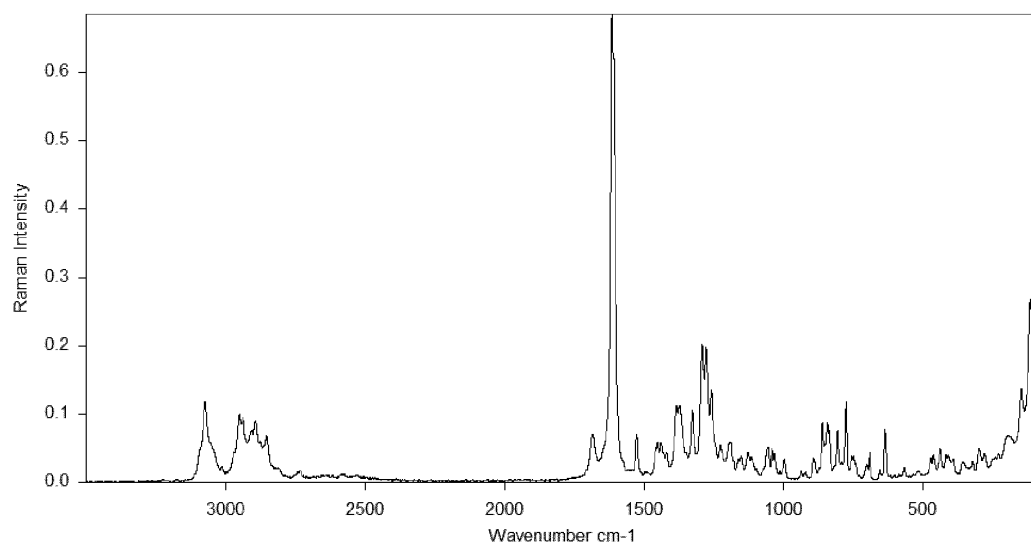


Fig. 13: Raman spectrum of the Monohydrate I, example 6b

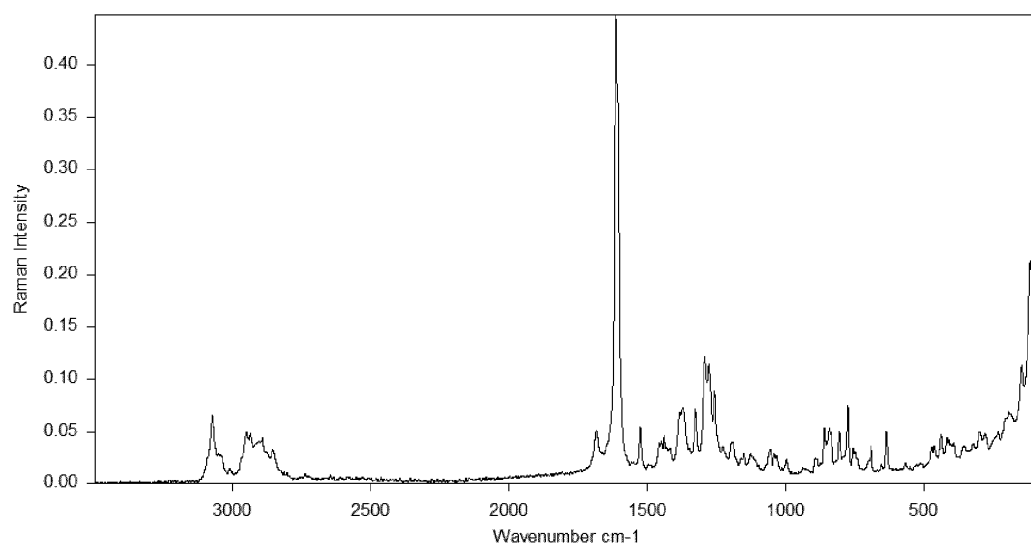
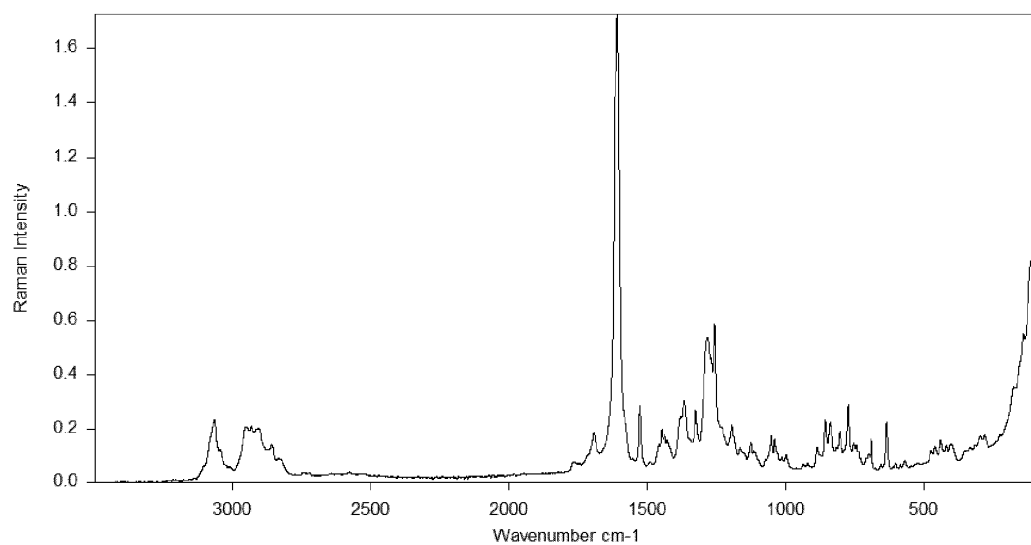
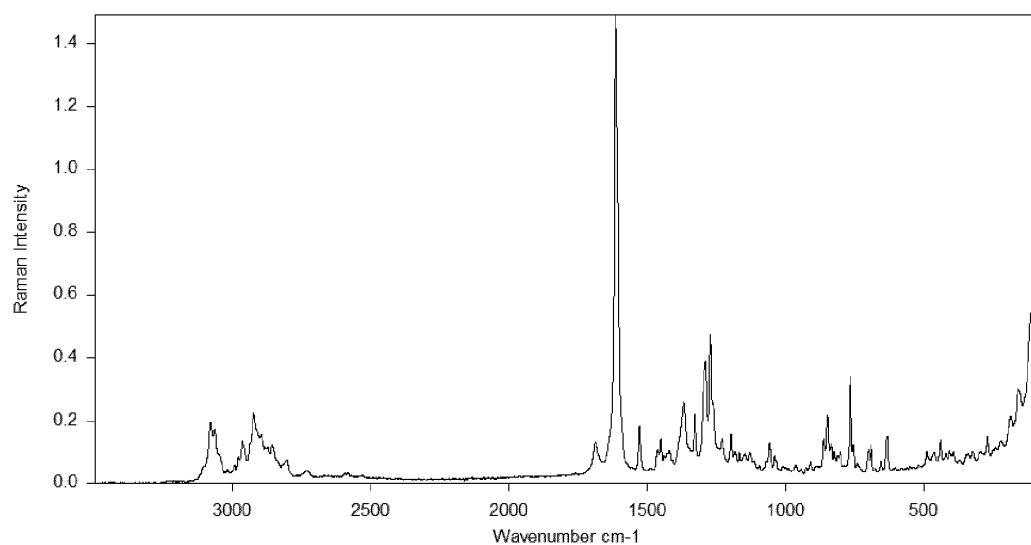


Fig. 14: Raman spectrum of the Monohydrate II, example 6c

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**Fig. 15:** Raman spectrum of the 1,25-Hydrate, example 6d**Fig. 16:** Raman spectrum of the Sesquihydrate, example 6e

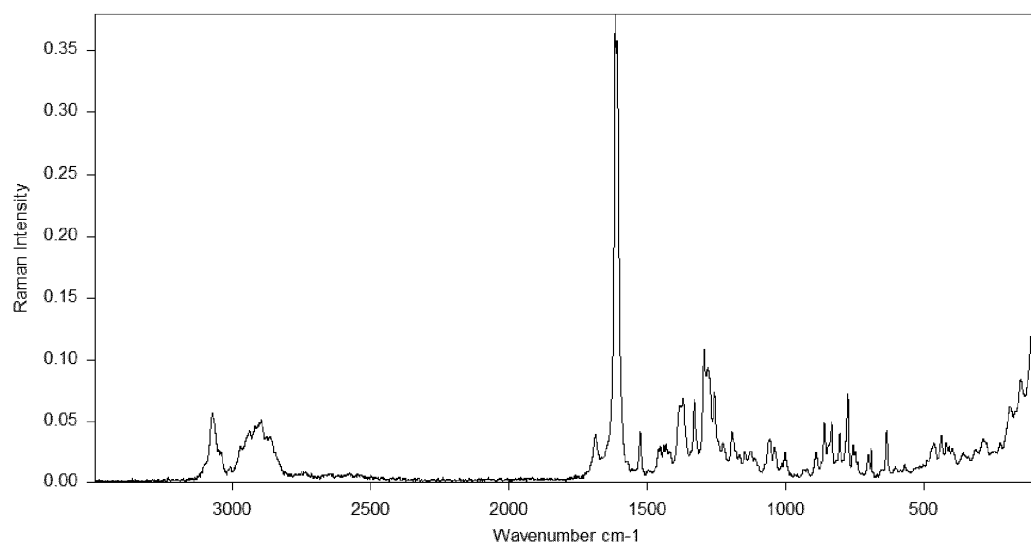


Fig. 17: Raman spectrum of the Dihydrate, example 6f

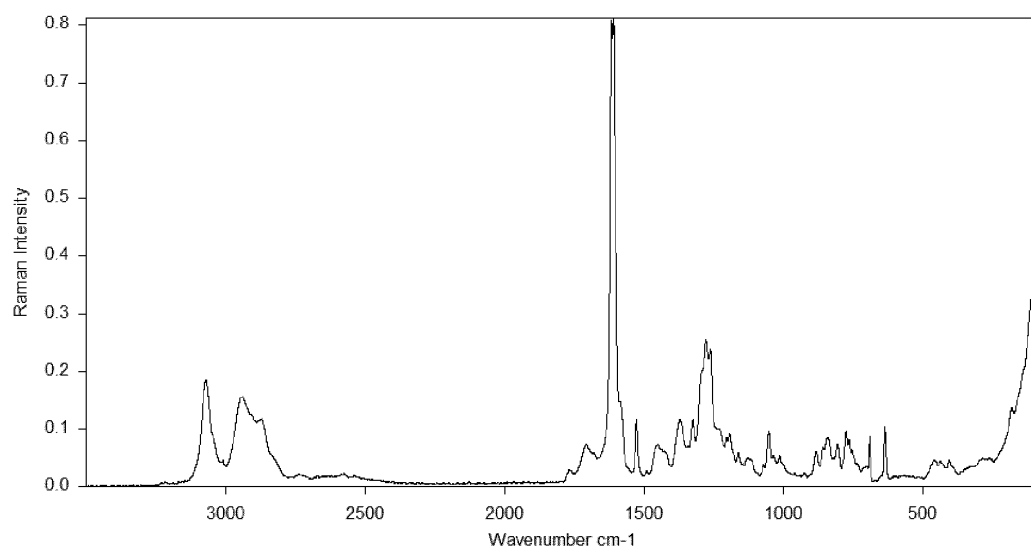
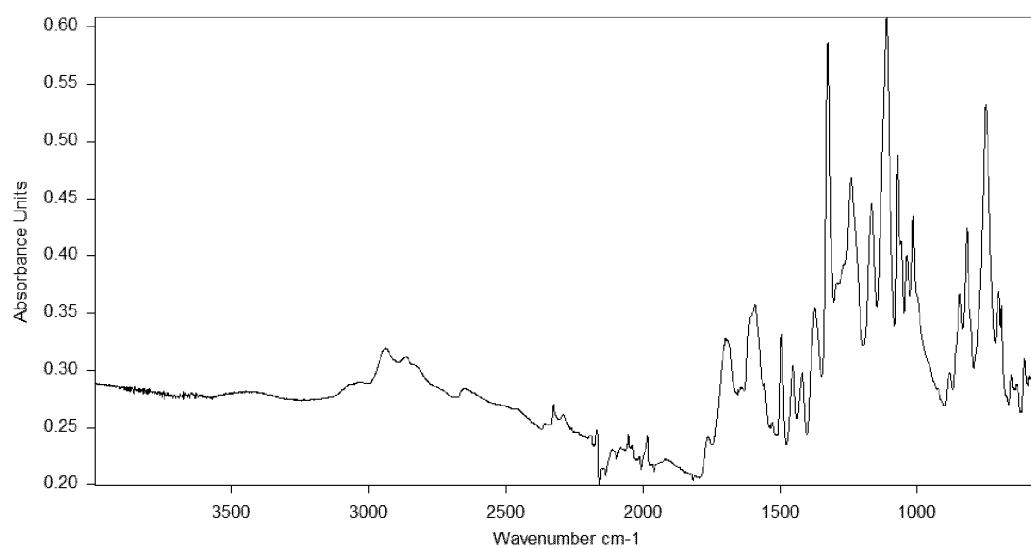
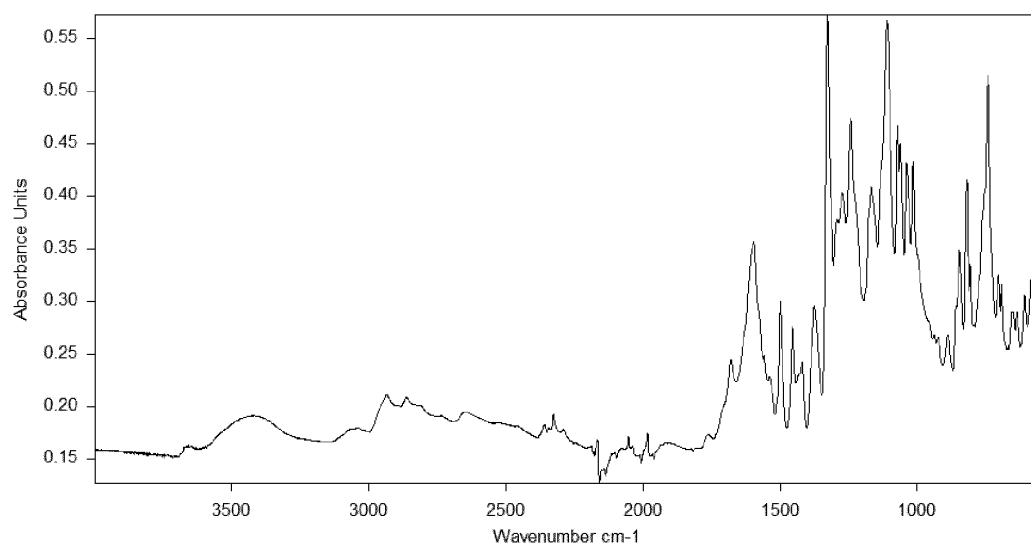


Fig. 18: Raman spectrum of the amorphous form, example 6g

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**Fig. 19:** IR spectrum of the Semihydrate, example 6a**Fig. 20:** IR spectrum of the Monohydrate I, example 6b

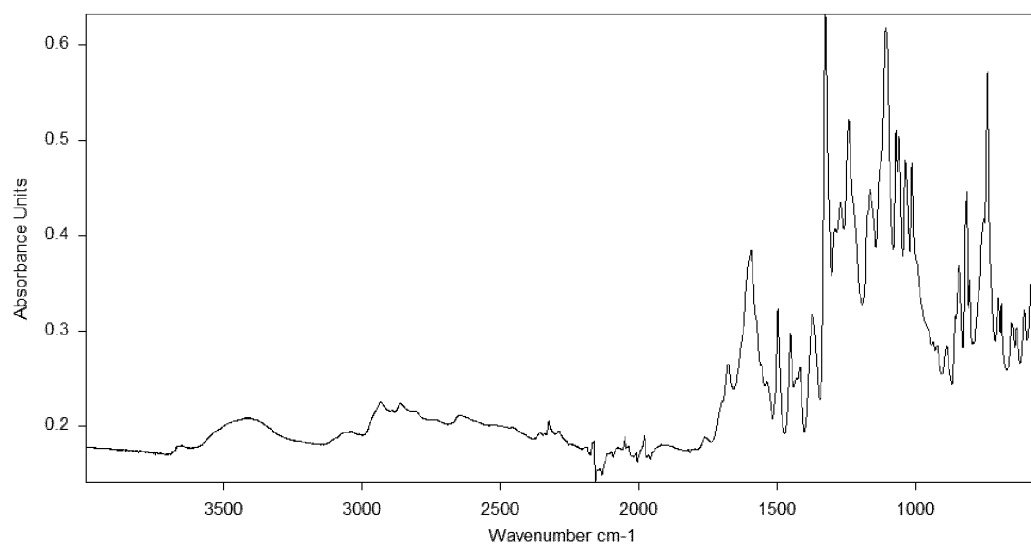


Fig. 21: IR spectrum of the Monohydrate II, example 6c

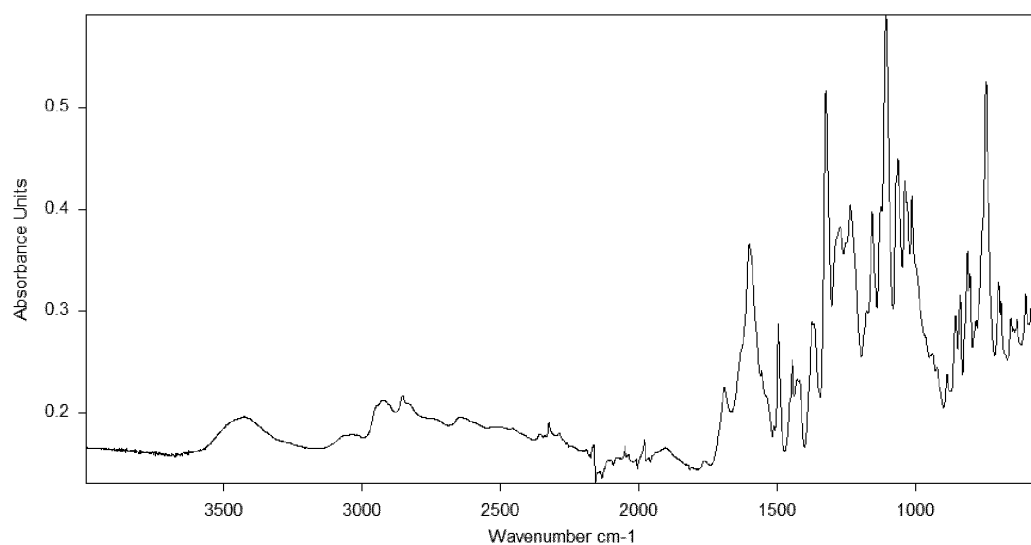


Fig. 22: IR spectrum of the 1,25-Hydrate, example 6d

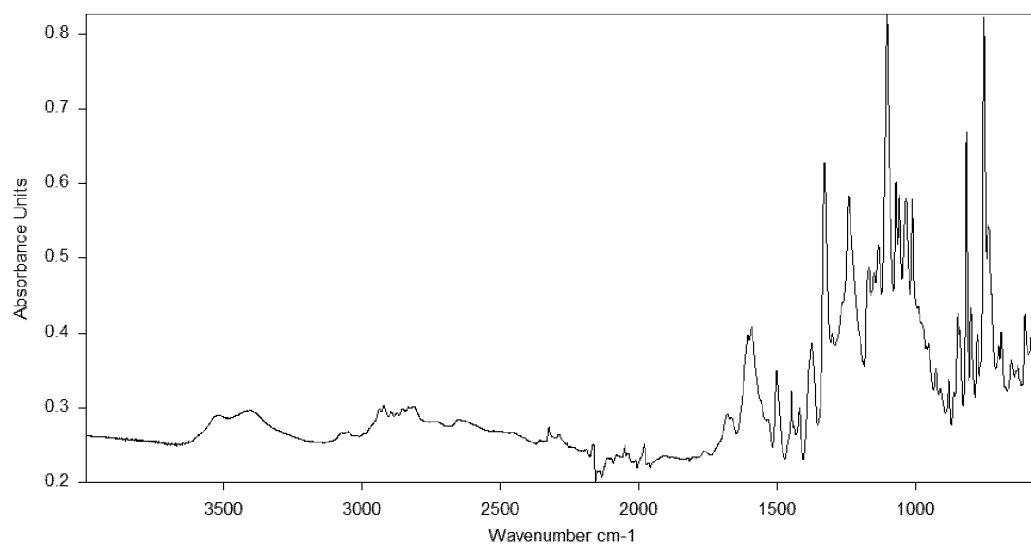


Fig. 23: IR spectrum of the Sesquihydrate, example 6c

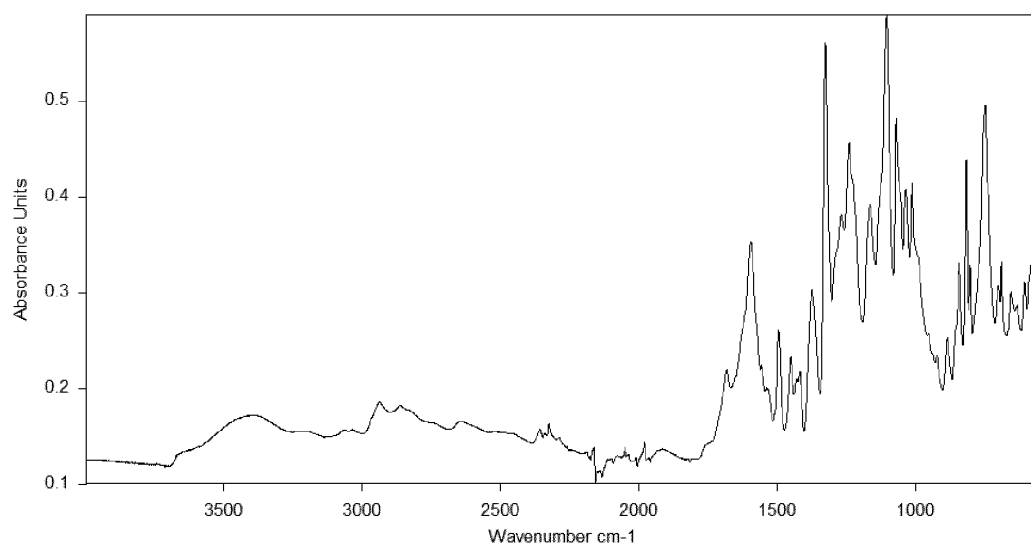


Fig. 24: IR spectrum of the Dihydrate, example 6f

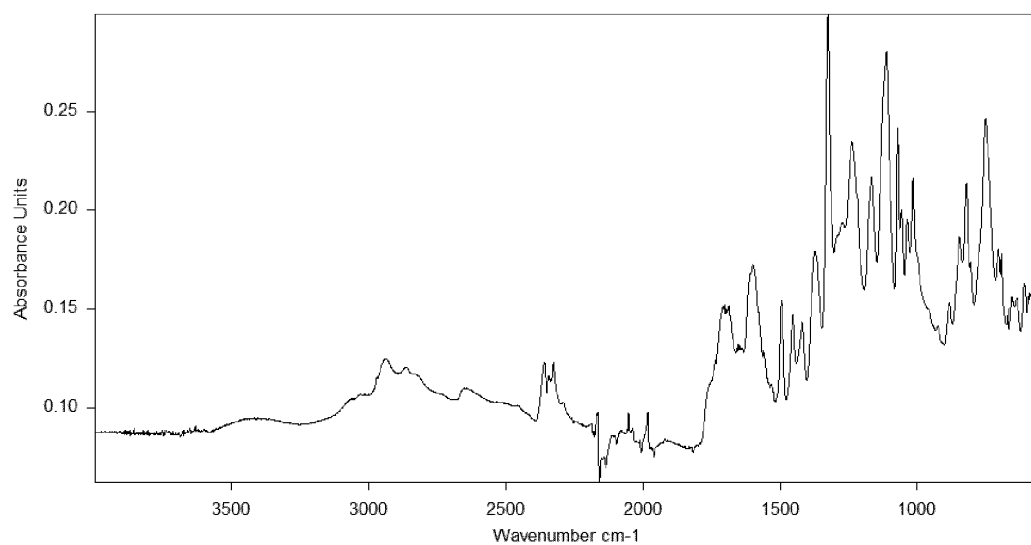


Fig. 25: IR spectrum of the amorphous form, example 6g

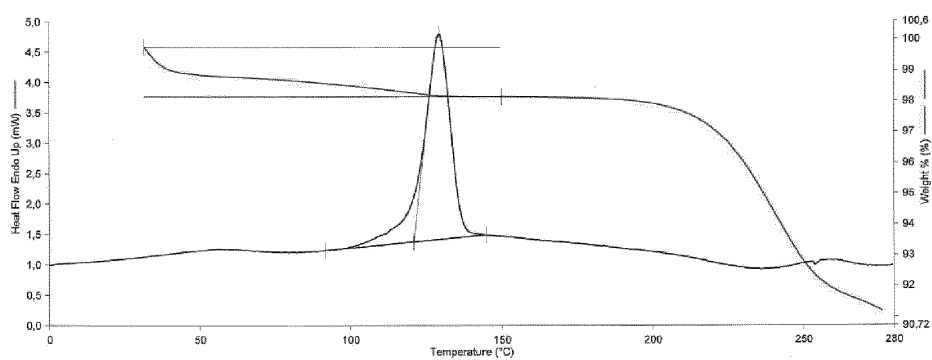
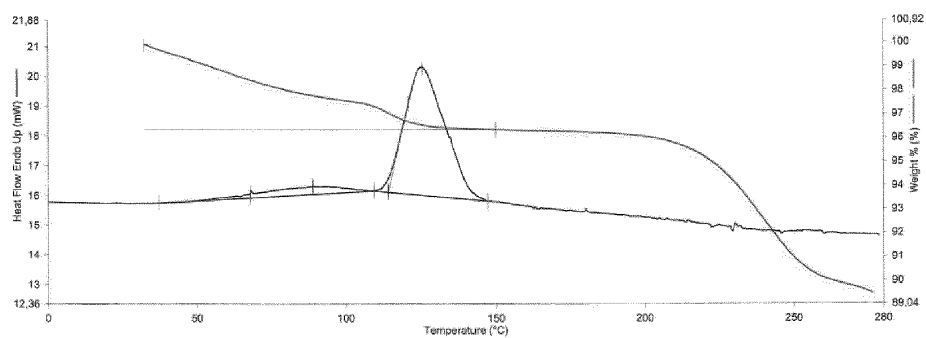
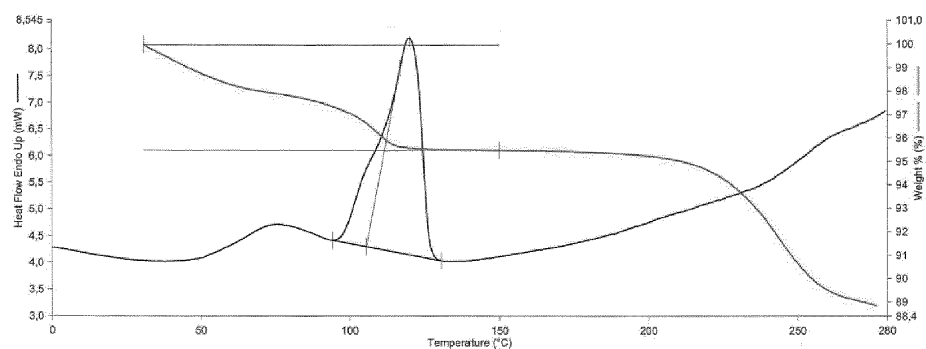
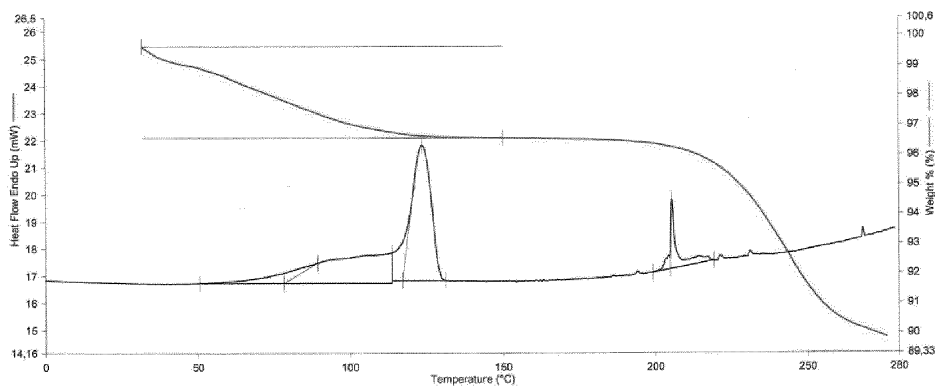
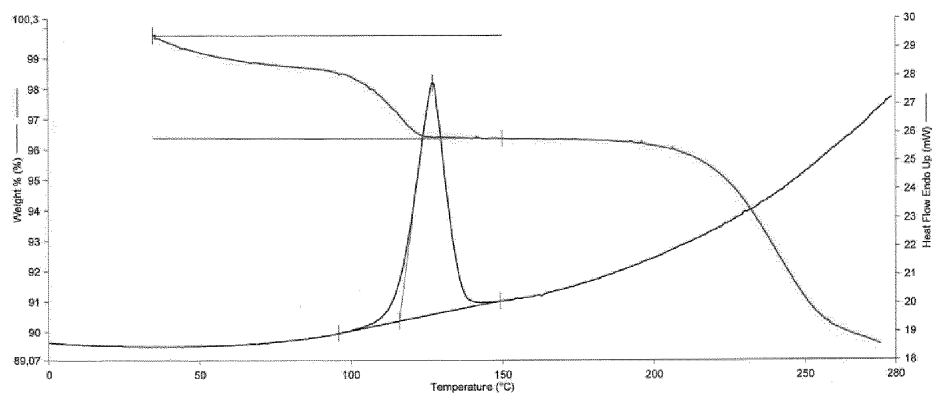


Fig. 26: DSC- and TGA-thermogram of the Semihydrate, example 6a

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**Fig. 27:** DSC- and TGA-thermogram of the Monohydrate I, example 6b**Fig. 28:** DSC- and TGA-thermogram of the Monohydrate II, example 6c

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**Fig. 29:** DSC- and TGA-thermogram of the 1,25-Hydrate, example 6d**Fig. 30:** DSC- and TGA-thermogram of the Sesquihydrate, example 6e

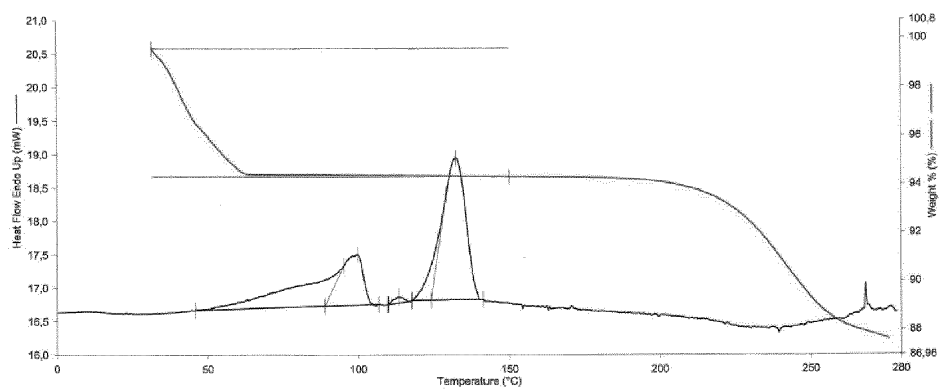


Fig. 31: DSC- and TGA-thermogram of the Dihydrate, example 6f

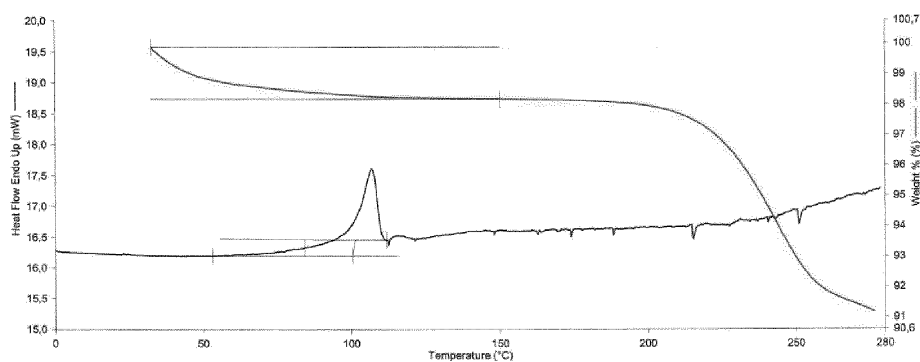


Fig. 32: DSC- and TGA-thermogram of the amorphous form, example 6g

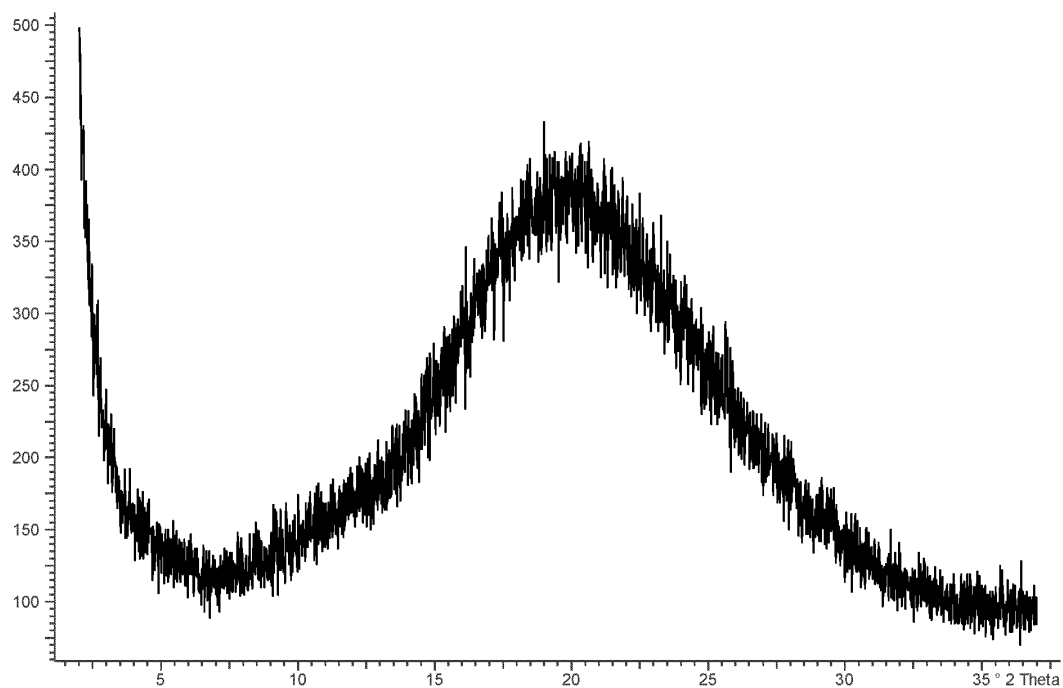


Fig. 33: X-Ray powder diffractogram of comparative example 11, amorphous form

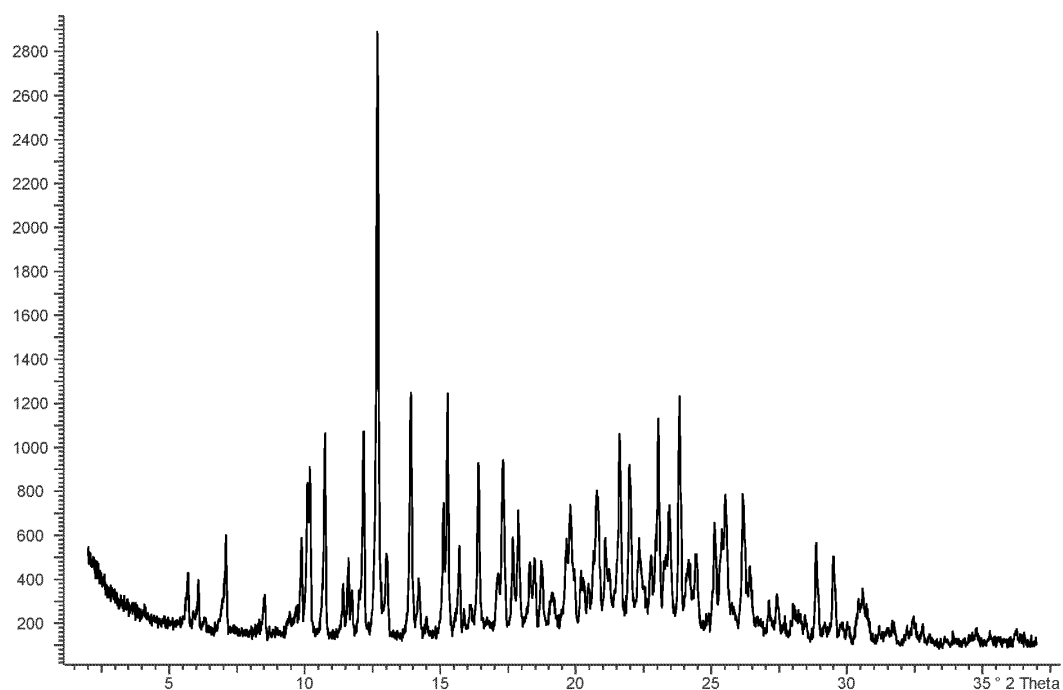


Fig. 34: X-Ray powder diffractogram of example 1, monohydrate II

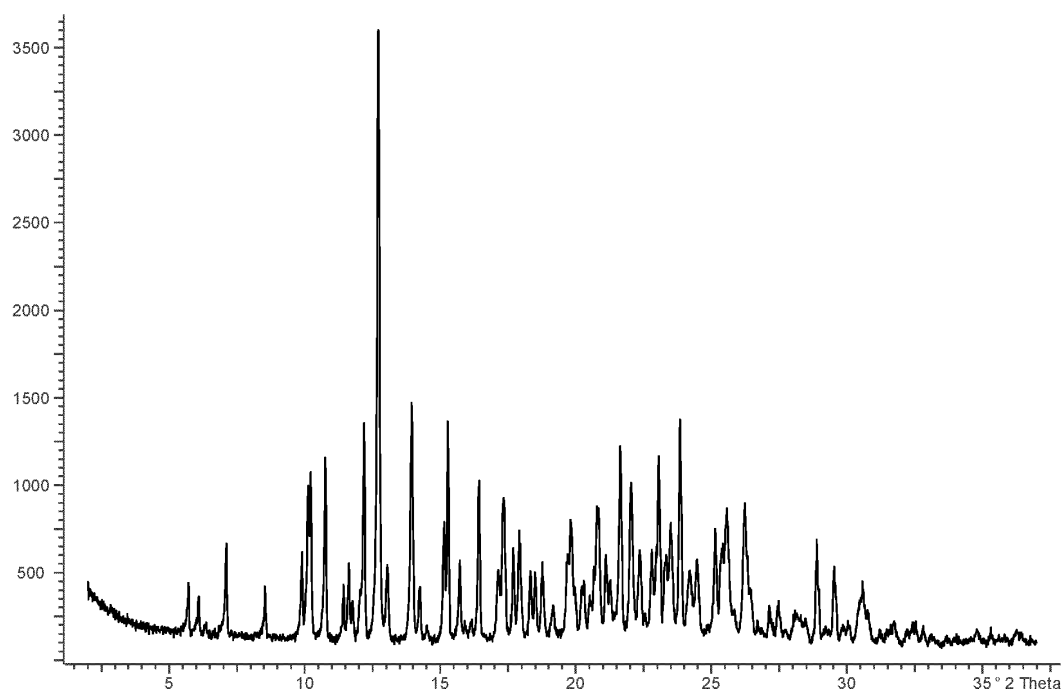


Fig. 35: X-Ray powder diffractogram of example 2 before micronization, monohydrate II

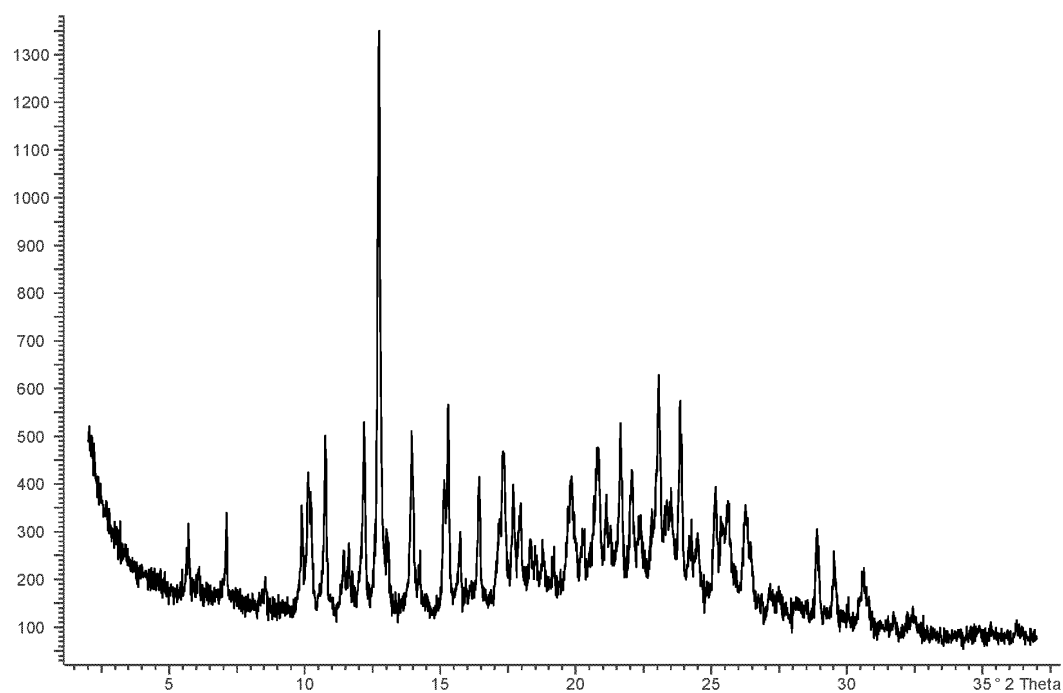


Fig. 36: X-Ray powder diffractogram of example 2 after micronization, monohydrate II, partial amorphization

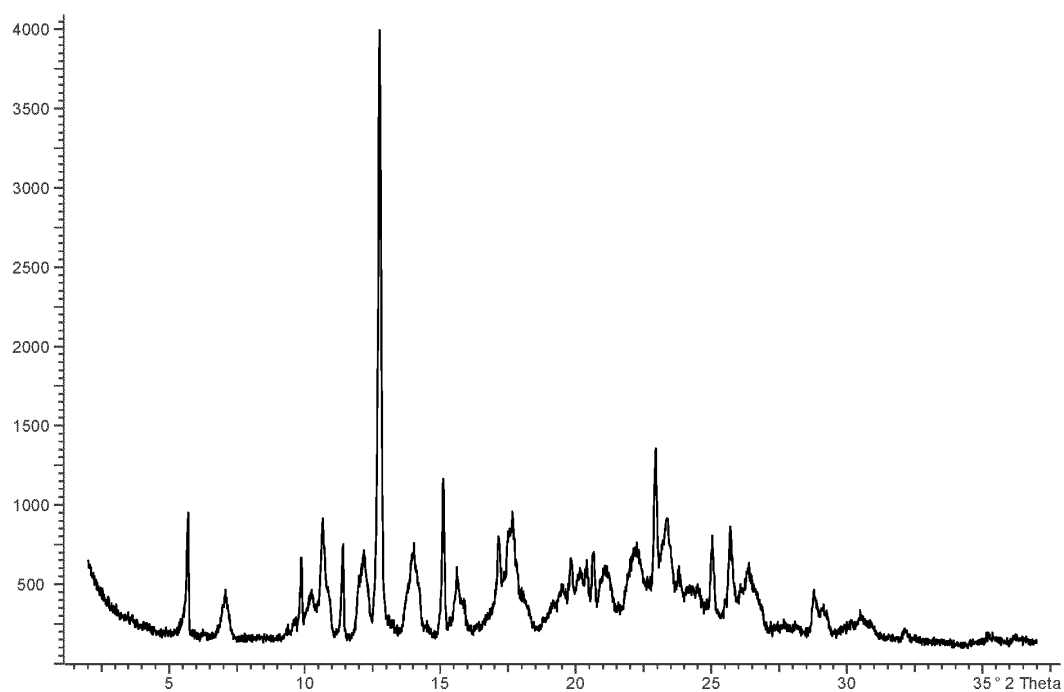


Fig. 37: X-Ray powder diffractogram of example 3, monohydrate I

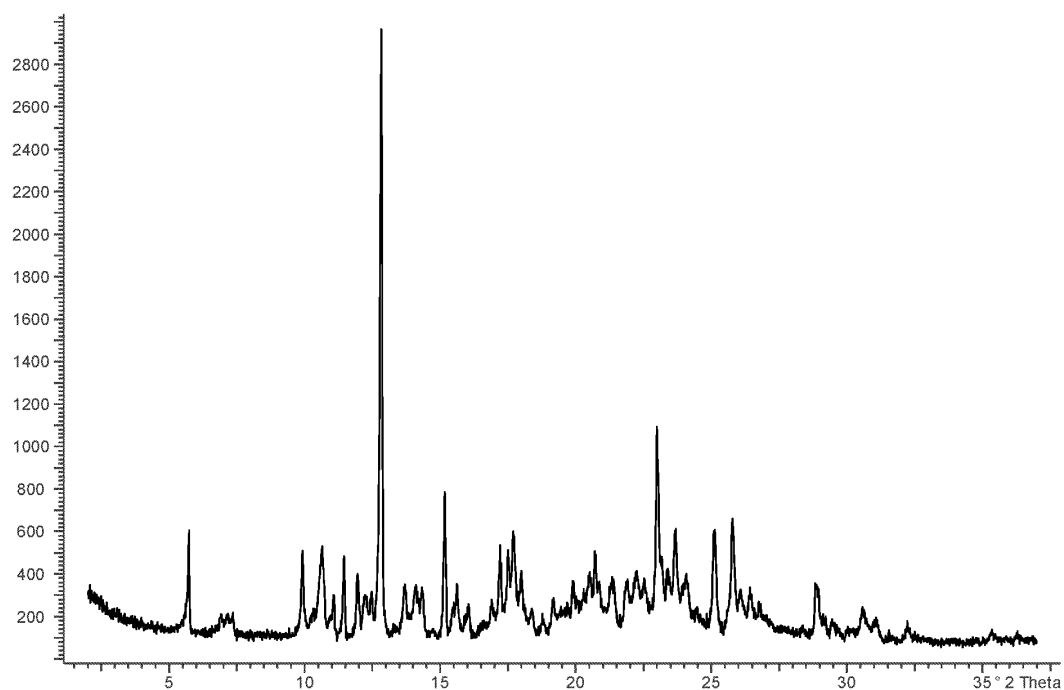


Fig. 38: X-Ray powder diffractogram of Example 4, monohydrate I

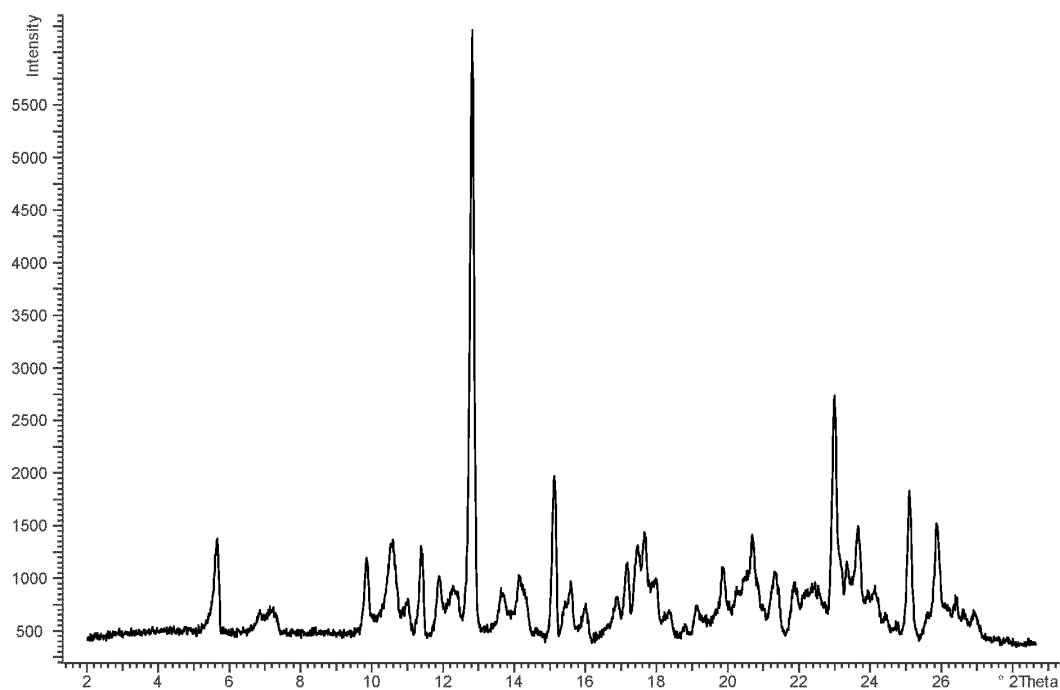


Fig. 39: X-Ray powder diffractogram of example 5, monohydrate I

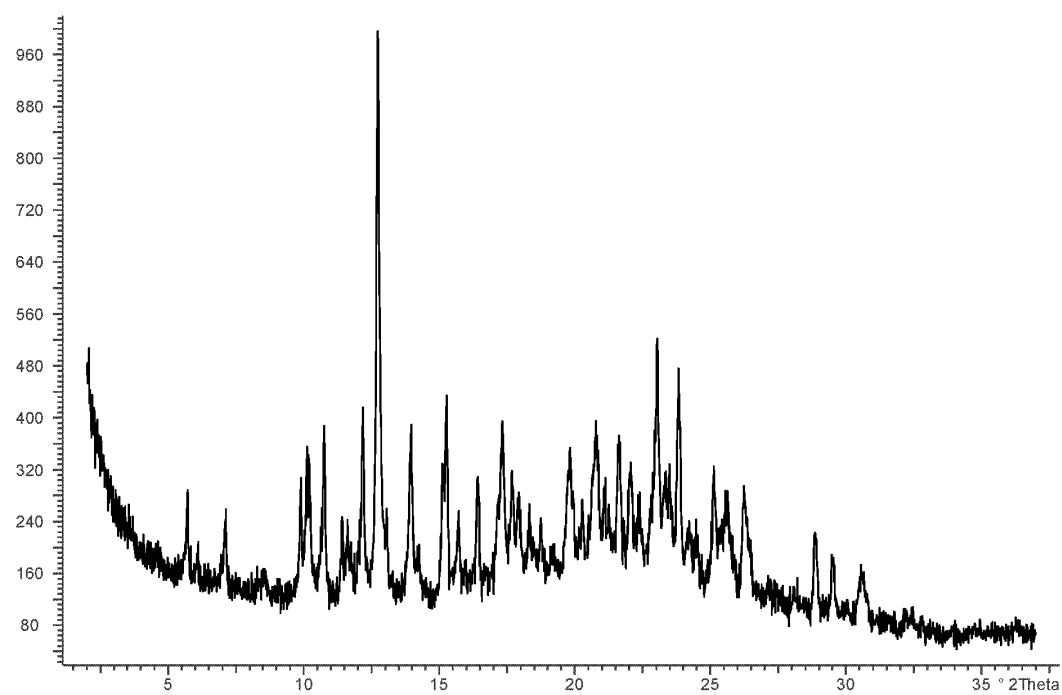


Fig. 40: X-Ray powder diffractogram of example 7 (storage stability): starting material for storage stability, monohydrate II

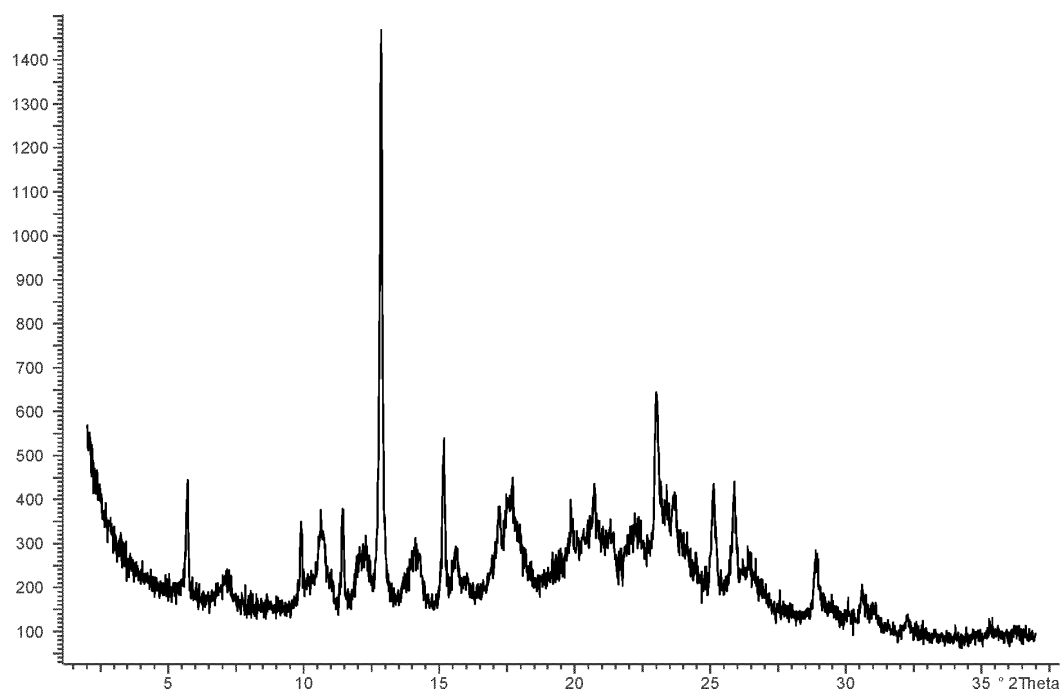


Fig. 41: X-Ray powder diffractogram of example 7b (storage stability): material after one month storage stability testing at 25°C and 60 % relative humidity in polyethylene, monohydrate I

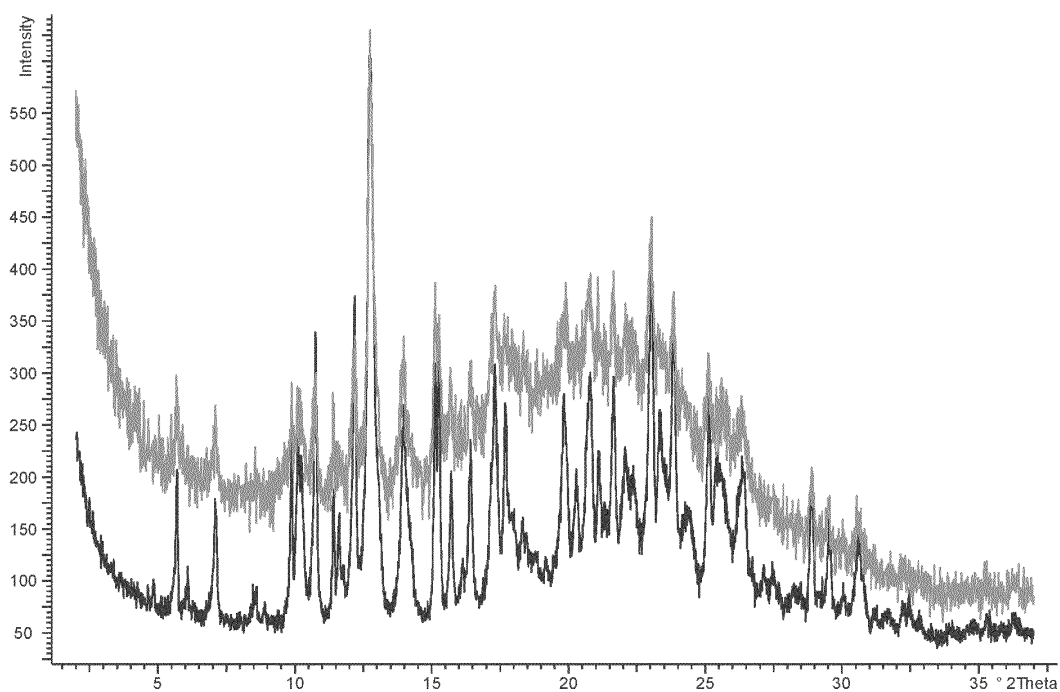


Fig. 42: Overlay of X-ray powder diffractograms of example 8b (micronization): starting material (monohydrate II) (base line) and material after micronization (monohydrate II with amorphous amounts, PTFE coated jet mill, 25°C) (top line)

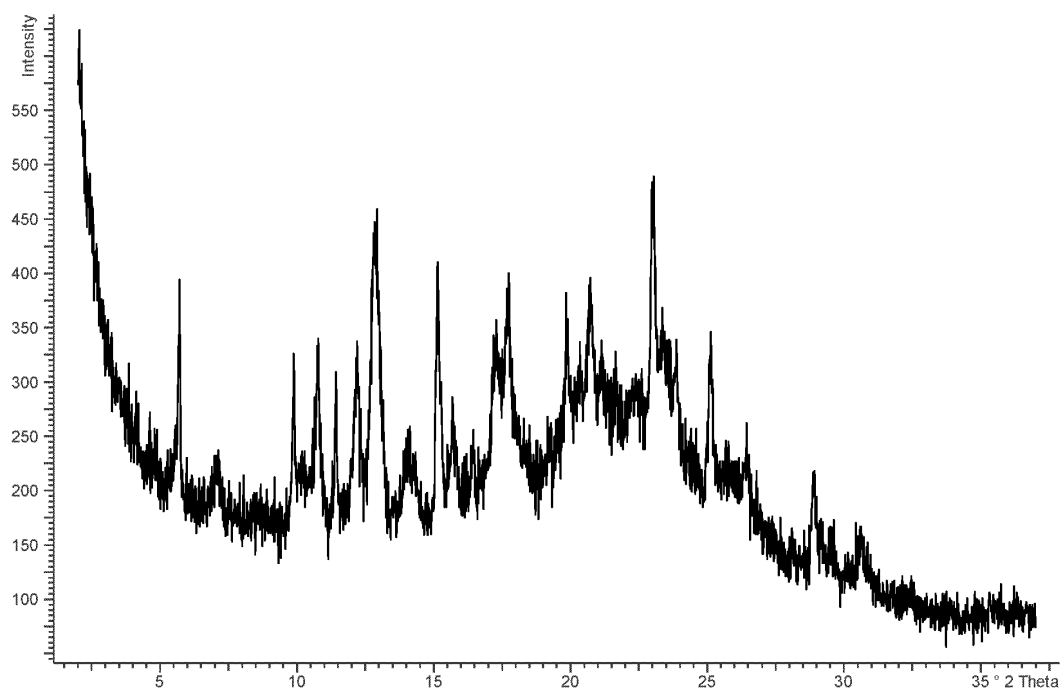


Fig. 43: X-ray powder diffractogram of example 8a: material after micronization (monohydrate I with amorphous amounts, VA jet mill, 25°C)

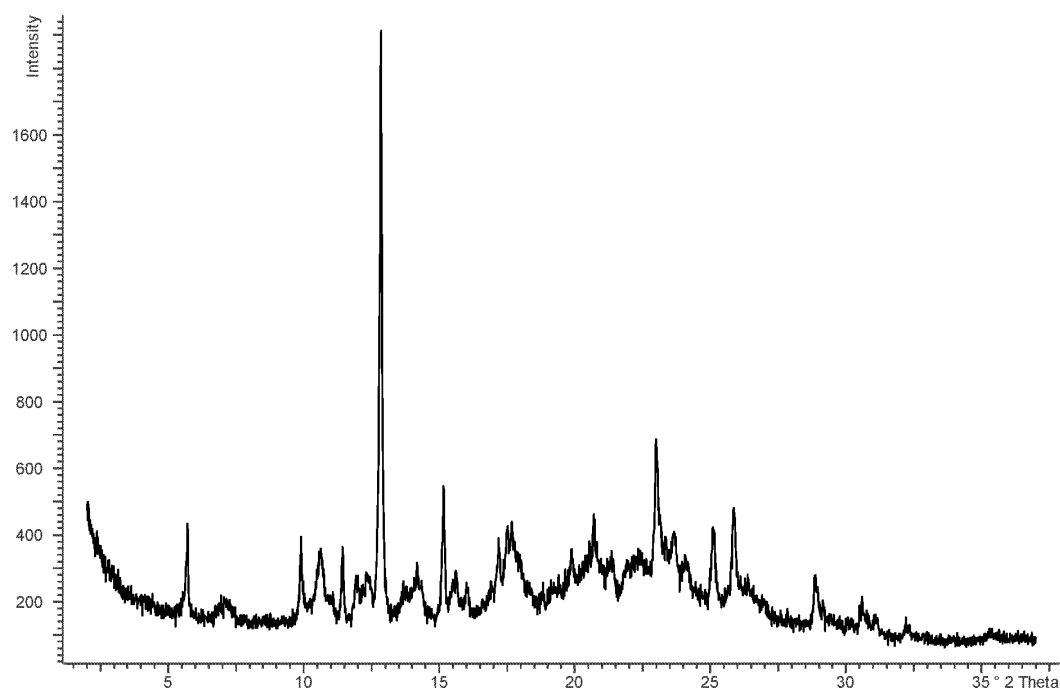


Fig. 44: X-ray powder diffractogram (example 8e): after micronization (monohydrate I)

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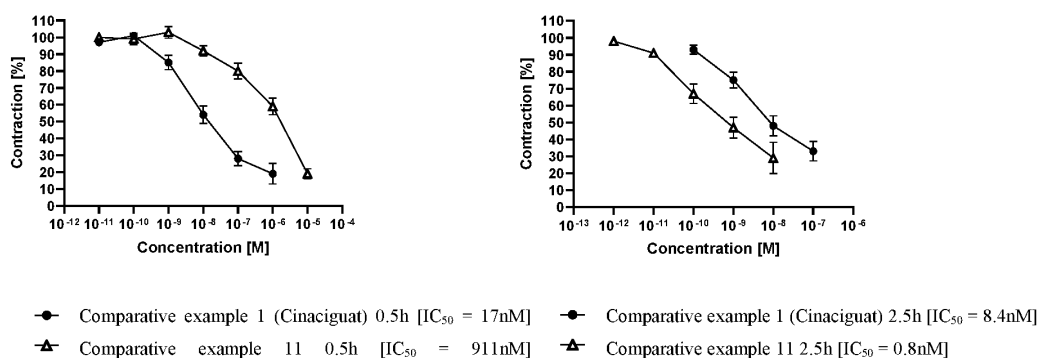


Fig. 45a + 45b: The effect of comparative example 11 in comparison to comparative example 1 (Cinaciguat) on PE-induced contraction of rabbit saphenous artery (incubation 0.5 h (left) vs. 2.5 h (right)). Data are presented as mean $\pm$ SEM

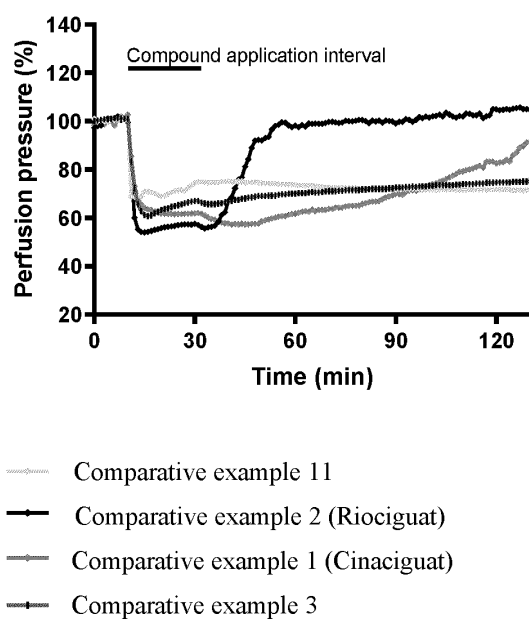


Fig. 46: Effects of comparative example 11 (300 nmol/l), comparative example 2 (100 nmol/l; Riociguat), comparative example 1 (100 nmol/l; Cinaciguat) and comparative example 3 (100 nmol/l) on coronary flow of isolated Langendorff-perfused rat heart and their wash-out. Data are presented as mean only.

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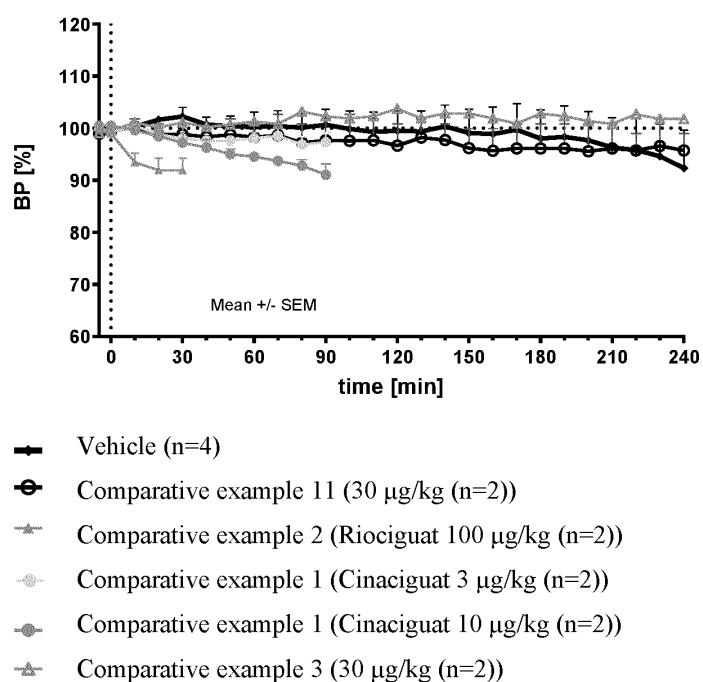


Fig. 47: Effects of vehicle solution, comparative example 11 (30 μ g/kg), comparative example 1 (Cinaciguat; 3 and 10 μ g/kg), comparative example 2 (Riociguat; 100 μ g/kg) and comparative example 3 (30 μ g/kg) after inhaled application under thromboxane analog U46619 induced PAH in minipigs on % changes in BP vs baseline (5min interval prior to start of nebulization). Data are mean $\pm$ SEM.

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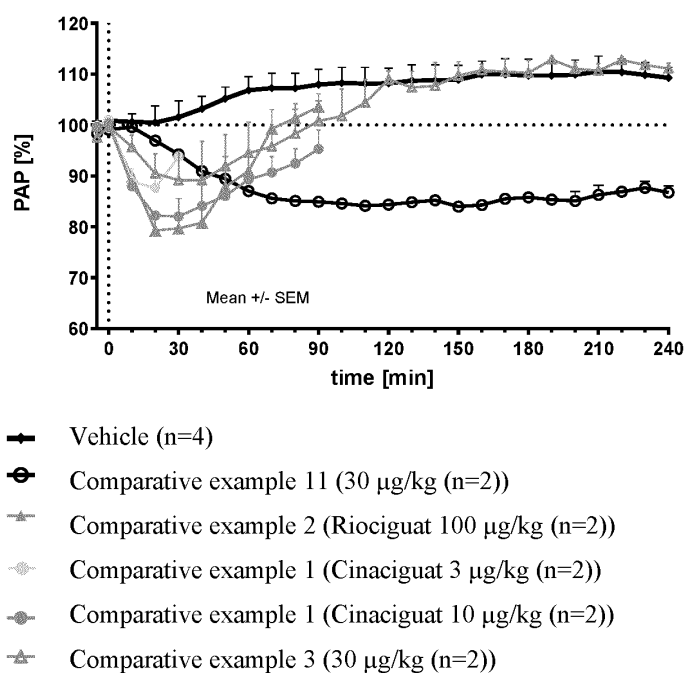
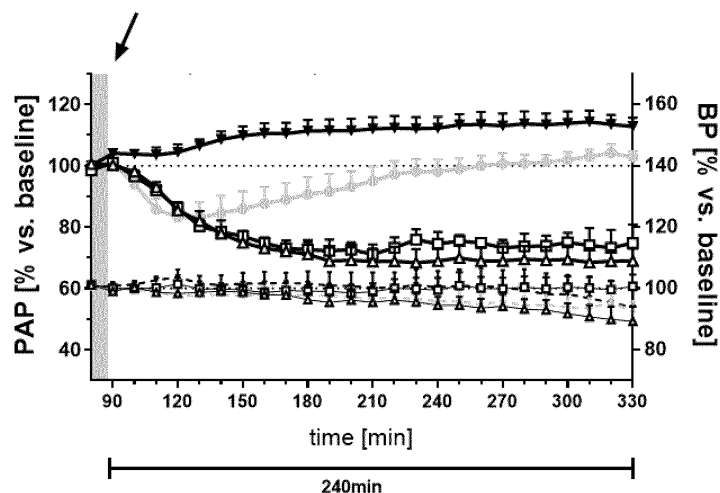


Fig. 48: Effects of vehicle solution, comparative example 11 (30 µg/kg), comparative example 1 (Cinaciguat; 3 and 10 µg/kg), comparative example 2 (Riociguat; 100 µg/kg) and comparative example 3 (30 µg/kg) after inhaled application under thromboxane analog U46619 induced PAH in minipigs on % changes in PAP vs baseline (5min interval prior to start of nebulization). Data are mean $\pm$ SEM.



↙ 5-7min Inhalation of Vehicle (n=4) or Comparative example 11 (n=3) or Comparative example 5 (n=3) or Comparative example 4 (n=3)

- PAP Vehicle
- ◆ PAP Comparative example 5 100 µg/kg
- PAP Comparative example 4 100 µg/kg
- ▲ PAP Comparative example 11 100 µg/kg
- - - BP Vehicle
- - - BP Comparative example 5 100 µg/kg
- - - BP Comparative example 4 100 µg/kg
- - - BP Comparative example 11 100 µg/kg

Fig. 49: Effects of vehicle solution, comparative example 11, comparative example 4 and comparative example 5 (all compounds at 100 µg/kg nominal dose) after inhaled application under thromboxane analog U46619 induced PAH in minipigs on % changes in PAP and BP vs baseline (5 min interval prior to start of nebulization). Data are mean ± SEM. Nebulization interval took 5-7 min for all compounds (yellow bar).

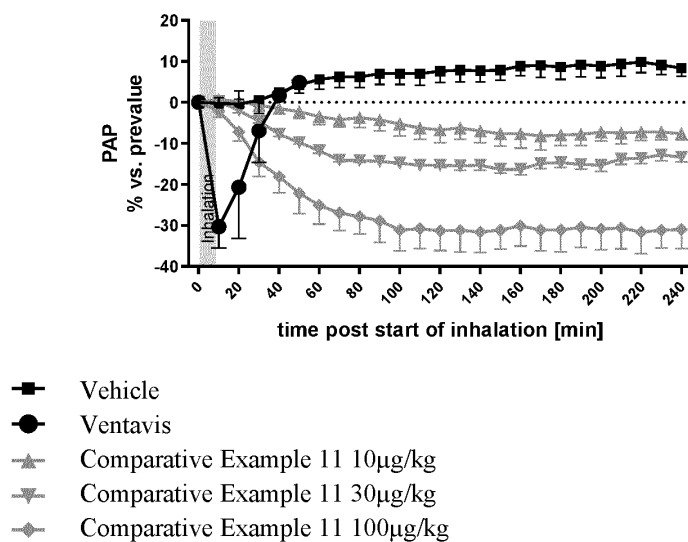
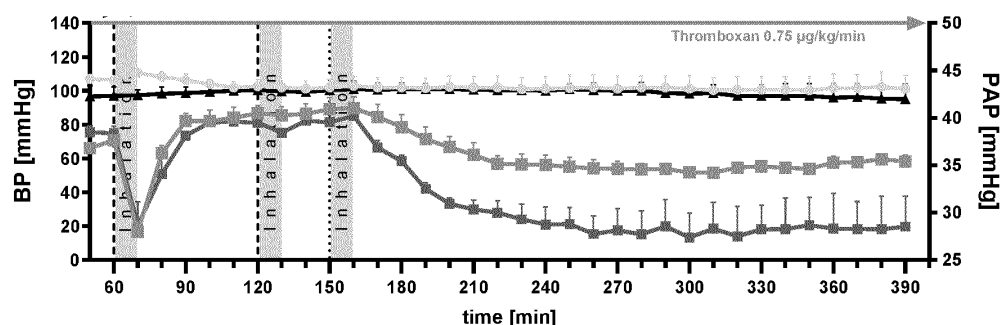


Fig. 50: Effects of vehicle solution, comparative example 11 (10, 30 and 100 µg/kg nominal dose) and Ventavis (10 µg/kg nominal dose) after inhaled application in the PAH minipigs model. Data are expressed as % changes in PAP and BP vs baseline (10 min interval prior to start of nebulization). Data are mean $\pm$ SEM. Nebulization interval took 5-7 min for all compounds (grey bar).

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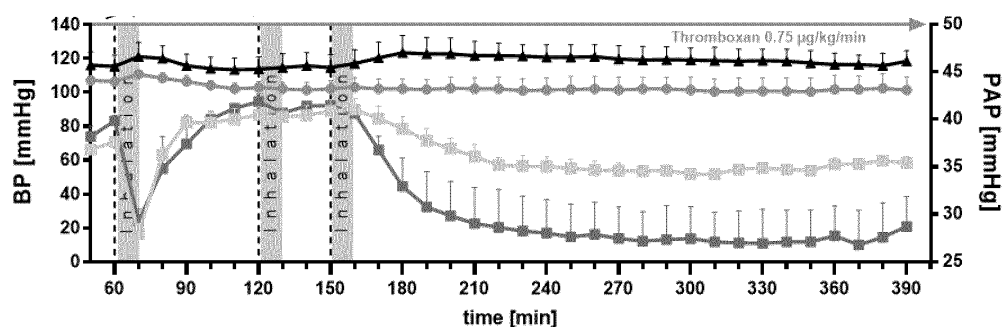


Inhalations: @60min: Ventavis 10µg/kg; @120min: Vehicle ;@150min: Comparative example 11 30µg/kg

○ BP wo ODQ ▲ BP with ODQ
 □ PAP wo ODQ ■ PAP with ODQ

Fig. 51: Effects of comparative example 11 after inhaled application under thromboxane analog U46619 induced PAH in minipigs with and without pretreatment by ODQ (1mg/kg iv). Data are mean $\pm$ SEM (n=3) BP: arterial blood pressure; bpm: beats per minute; HR: heart rate; iv: intravenous; mBP: mean blood pressure; mPAP: mean pulmonary artery pressure; ODQ: 1H-[1,2,4] Oxadiazolo[4,3-a]quinoxalin-1-one, a highly selective, irreversible, heme-site inhibitor of soluble guanylyl cyclase; PAH: pulmonary arterial hypertension; PAP: pulmonary artery pressure; SEM: standard error of the mean; w/wo: with/without; wo: without

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Inhalations: @60min: Ventavis 10 μ g/kg; @120min: Vehicle ;@150min: Comparative example 11 30 μ g/kg

● BP wo L-NAME ■ PAP with L-NAME
 ○ PAP wo L-NAME ▲ BP with L-NAME

Fig. 52: Effects of comparative example 11 after inhaled application under thromboxane analog U46619 induced PAH in minipigs with and without pretreatment by L-NAME (10mg iv. Bolus followed by 5 mg/kg/h infusion). Data are mean $\pm$ SEM (n=3) iv.: intravenous; L-NAME: L-N ω -Nitroarginine methyl ester; mBP: mean blood pressure; mPAP: mean pulmonary artery pressure; PAH: pulmonary arterial hypertension; PAP: pulmonary artery pressure; SEM: standard error of the mean; w/wo: with/without; wo: without

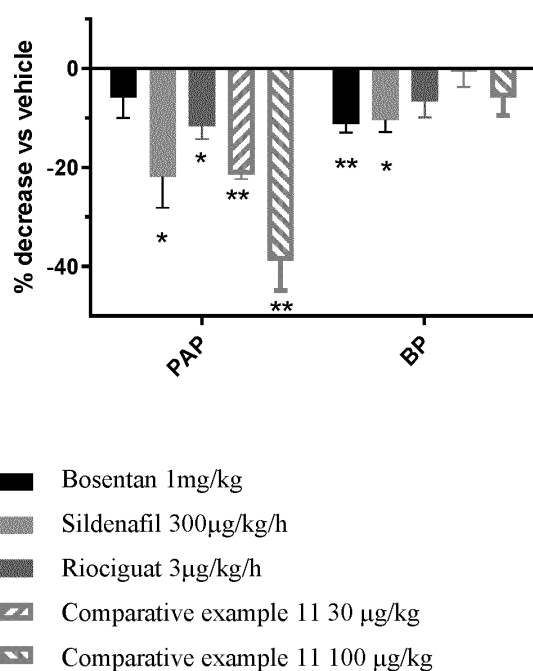


Fig. 53a: Effects on % decrease in PAP and BP of comparative example 11 (30 and 100 µg/kg nominal dose) after inhaled application compared to systemically applied bosentan (1mg/kg), sildenafil (300 µg/kg/h) and riociguat (3 µg/kg/h) under thromboxane analog U46619 induced PAH in minipigs. Data are mean $\pm$ SEM (n=3)

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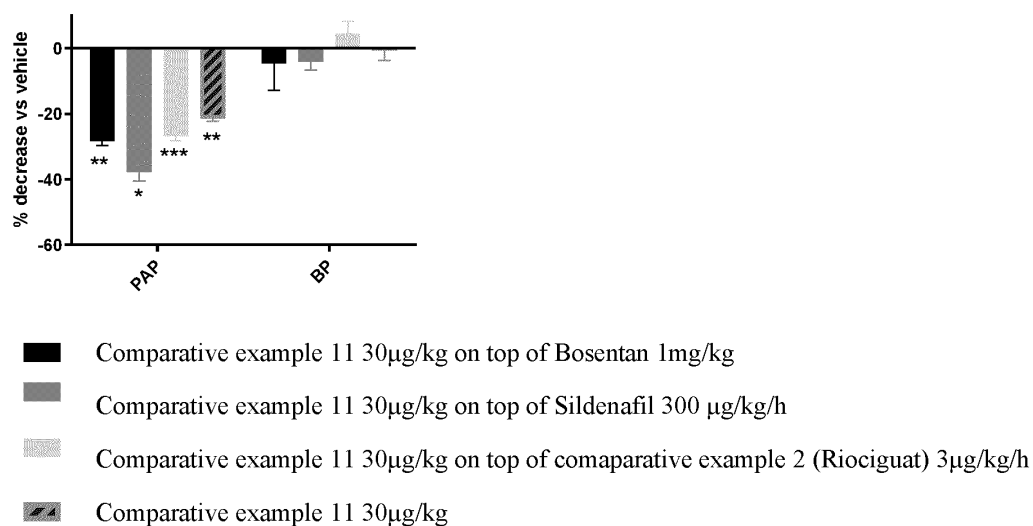
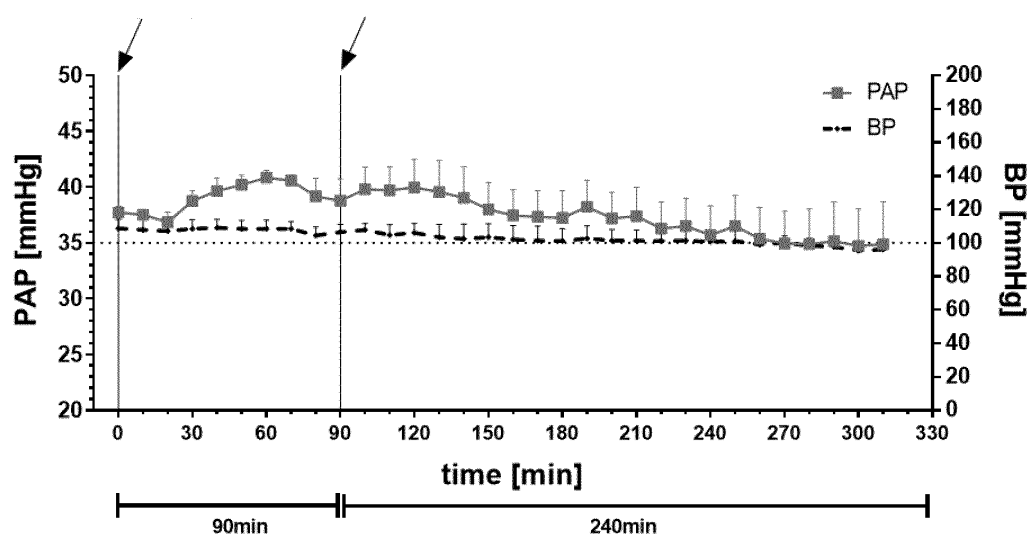


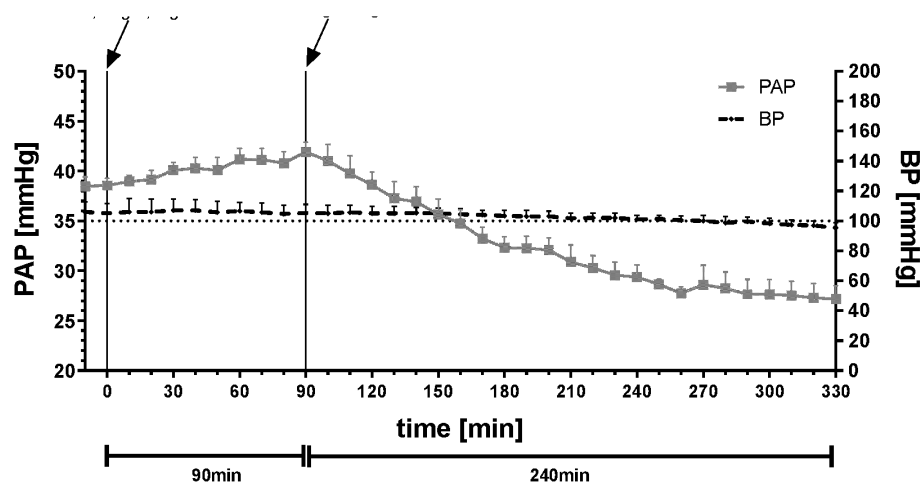
Fig. 53b: Effects on % decrease in PAP and BP of comparative example 11 (30 µg/kg nominal dose) after inhaled application alone or on top of systemically applied bosentan (1mg/kg), sildenafil (300 µg/kg/h) and riociguat (3 µg/kg/h) under thromboxane analog U46619 induced PAH in minipigs. Data are mean ± SEM (n=3)



↙ @0 min: Lactose 1.5mg/4kg; @90 min: Lactose formulation I (2%) 1.5mg/4kg

Fig. 54: Effects of lactose as well as lactose formulation I (7.5 μ g/kg) after intratracheal application. Data are mean $\pm$ SEM (n=3); Intratracheal application was conducted with PennCentury dry powder insufflator and Air Pump; BP: arterial blood pressure; PAP: pulmonary artery pressure; SEM: standard error of the mean

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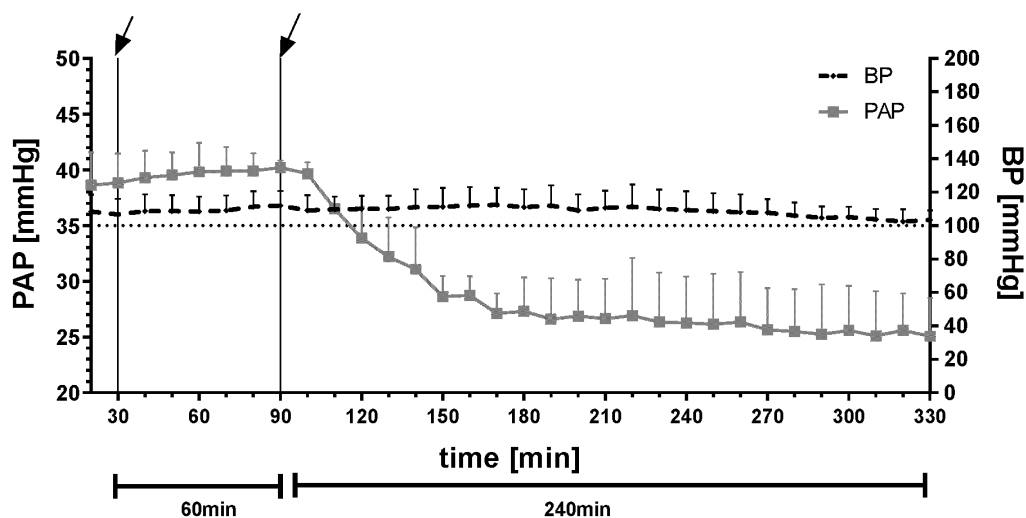


↙ @0 min: Lactose 1.5mg/4kg; @90 min: Lactose formulation II (6%) 1.5mg/4kg

Fig. 55: Effects of lactose as well as lactose formulation II (22.5 μ g/kg) after intratracheal application.

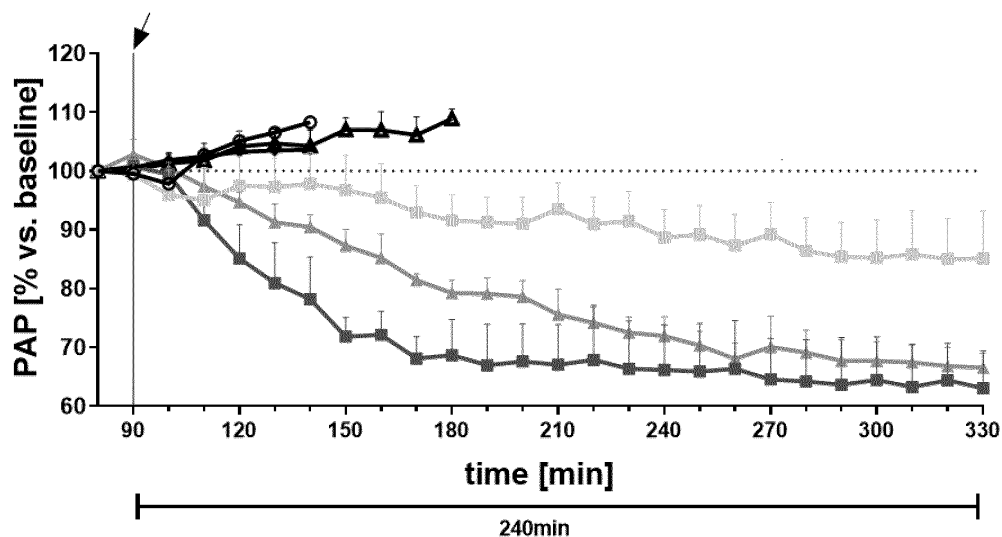
Data are mean $\pm$ SEM (n=3); Intratracheal application was conducted with PennCentury dry powder insufflator and Air Pump; BP: arterial blood pressure; PAP: pulmonary artery pressure; SEM:

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↙ @30 min: Lactose 1.5mg/4kg; @90 min: micronized example 6e 1.5mg/4kg

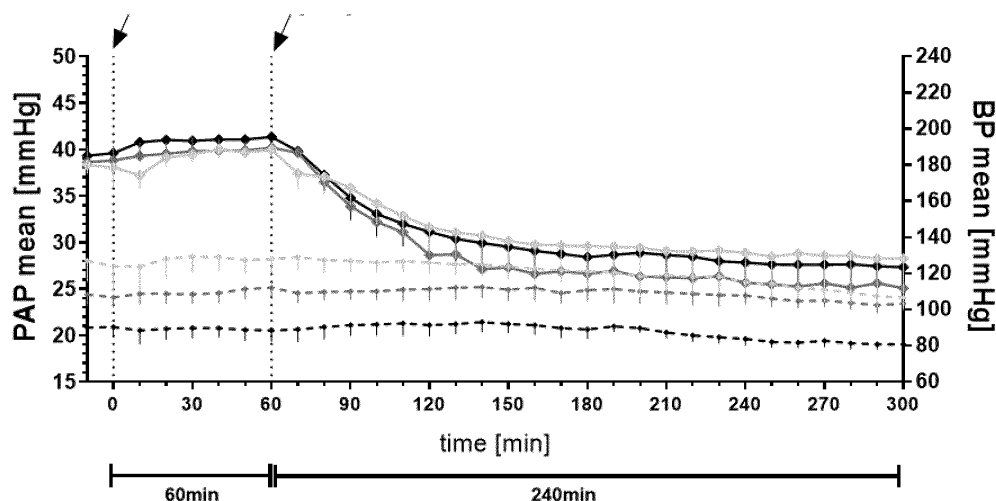
Fig. 56: Effects of lactose and micronized sesquihydrate, e.g. ex.. 6e (375 μ g/kg) after intratracheal application. Data are mean $\pm$ SEM (n=3) Intratracheal application was conducted with PennCentury dry powder insufflator and Air Pump; BP: arterial blood pressure; PAP: pulmonary artery pressure; SEM: standard error of the mean



↙ @90 min: Example 6e (mikro.) or lactose formulation I or II (2 or 6%) or Lactose 1.5mg/4kg

- PAP Lactose LH300/LH200 20:78m/m
- ▲ PAP Lactose LH300/LH200 20:80m/m
- PAP Lactose LH300/LH200 20:80m/m
- PAP Lactose formulation I (2%)
- ▴ PAP Lactose formulation II (6%)
- PAP Micronized example 6e

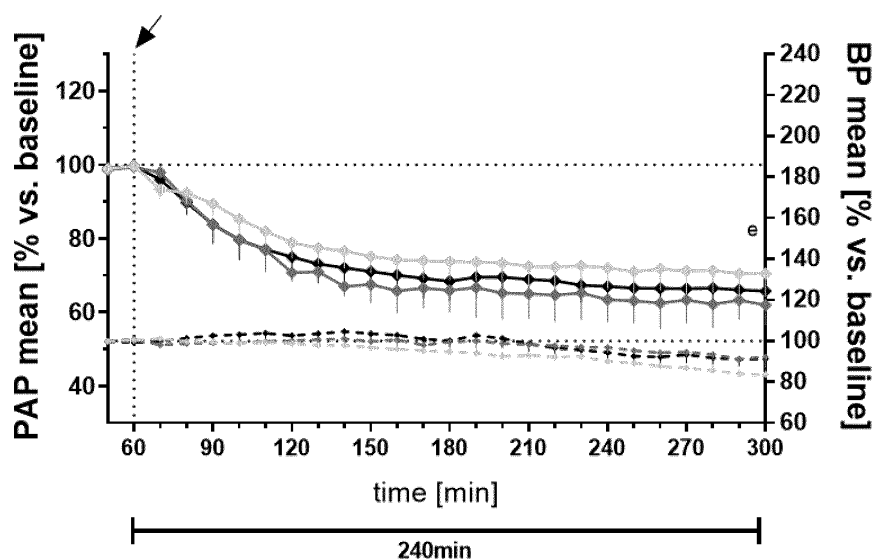
Fig. 57: Effects of intratracheal application of different lactose vehicles, lactose formulation I (7.5 µg/kg), lactose formulation II (22.5 µg/kg) and micronized sesquihydrate example 6e (375 µg/kg). Data are shown as %changes vs. prevalues as mean ± SEM (n=3)



↙ @0 min: Lactose LH300/LH200 1.5mg/4kg @60min: Hydrates of comparative example 11
micronized 1.5mg/4kg

- ◆— PAP mean example 2 Monohydrate (n=3)
- ◆— BP mean example 2 Monohydrate (n=3)
- ◆— PAP mean Semihydrate in analogy to example 6a (n=3)
- ◆— BP mean Semihydrate in analogy to example 6a (n=3)
- ◆— PAP mean Sesquihydrate in analogy to example 6e (n=3)
- ◆— BP mean Sesquihydrate in analogy to example 6e (n=3)

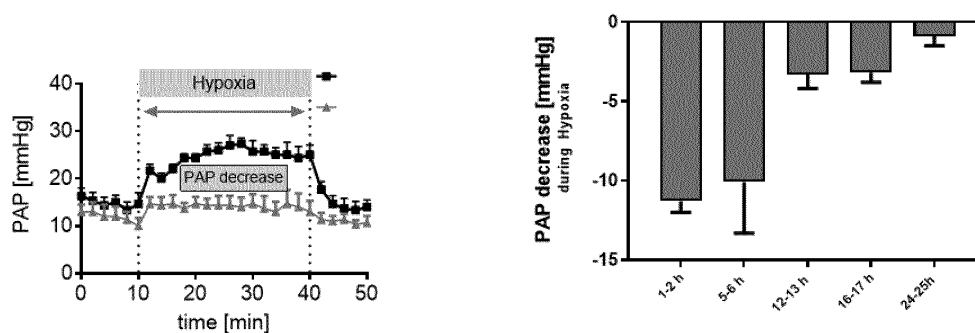
Fig. 58: Effects of comparative example 11 after intratracheal application of different hydrates micronized monohydrate II (example 2), micronized semihydrate (example 6a) and micronized sesquihydrate (example 6e), on BP and PAP. Data are shown as absolute values [mmHg] as mean $\pm$ SEM (n=3)



↙ @60 min: Hydrates of comparative example 11 micronized 1.5mg/4kg

- ◆— PAP mean example 2 Monohydrate (n=3)
- -◆- - BP mean example 2 Monohydrate (n=3)
- PAP mean Semihydrate in analogy to example 6a (n=3)
- -■- - BP mean Semihydrate in analogy to example 6a (n=3)
- ▲— PAP mean Sesquihydrate in analogy to example 6e (n=3)
- -▲- - BP mean Sesquihydrate in analogy to example 6e (n=3)

Fig. 59: Effects of comparative example 11 after intratracheal application of different hydrates micronized monohydrate II (example 2), micronized semihydrate (example 6a) and micronized sesquihydrate (example 6e), on BP and PAP. Data are shown as absolute values [mmHg] as mean $\pm$ SEM (n=3)



■ Placebo
 ▲ Comparative example 11 100 µg/kg

Fig. 60 a and 60b: Fig. 60a (left side): 5-6h after inhalation: PAP decrease for each animal is calculated as followed: $\text{PAP decrease} = (\text{SUM of mPAP from 10-40min of Comparative example 11 treated animal}) - (\text{SUM of mPAP from 10-40min of respective Placebo treated animal}) / \text{number of time points}$; Fig. 60b: (right side): Effects of comparative example 11 (100 µg/kg nominal dose) after inhaled application 1, 5, 12, 16 and 24 hours before hypoxia on hypoxia induced PAP increase in conscious dogs. Data are shown as mean ± SEM (n=3)

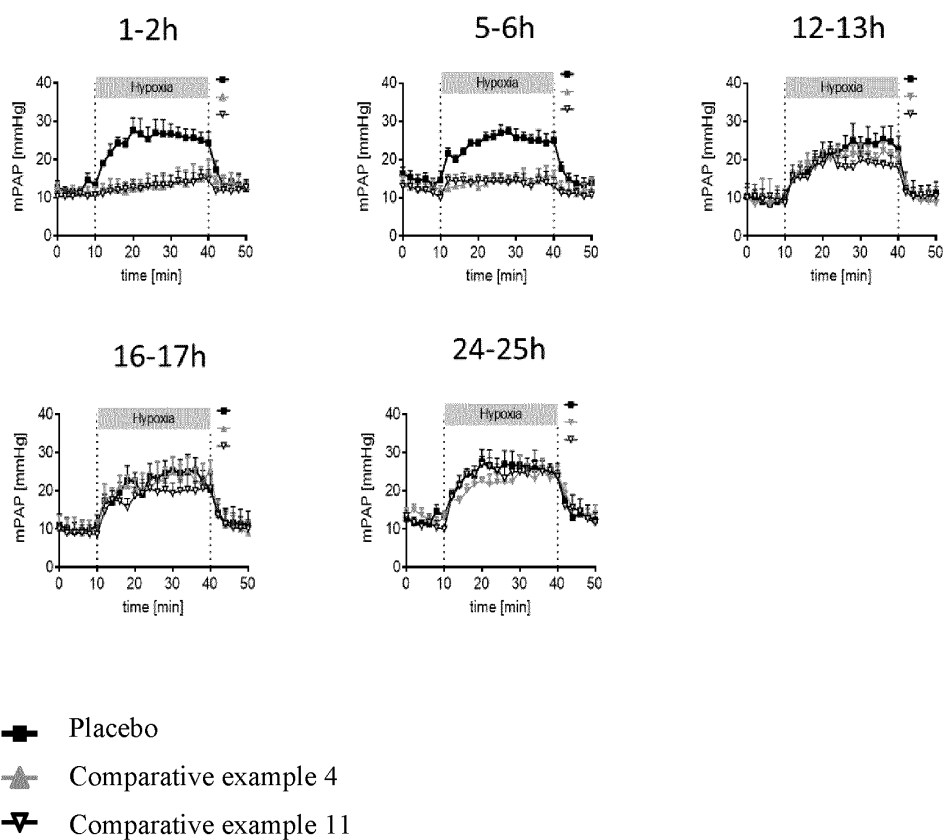


Fig. 61a-61e: Hemodynamic effects of comparative example 11 and comparative example 4 (100 $\mu\text{g/kg}$ nominal dose) after inhaled application 1, 5, 12, 16 and 24 hours before hypoxia on hypoxia induced PAP increase in conscious dogs. Data are shown as mean $\pm$ SEM (n=3)

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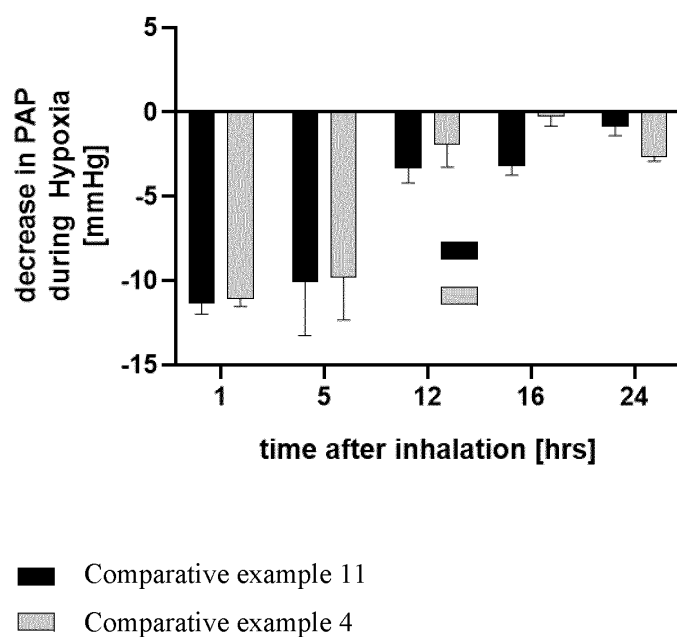
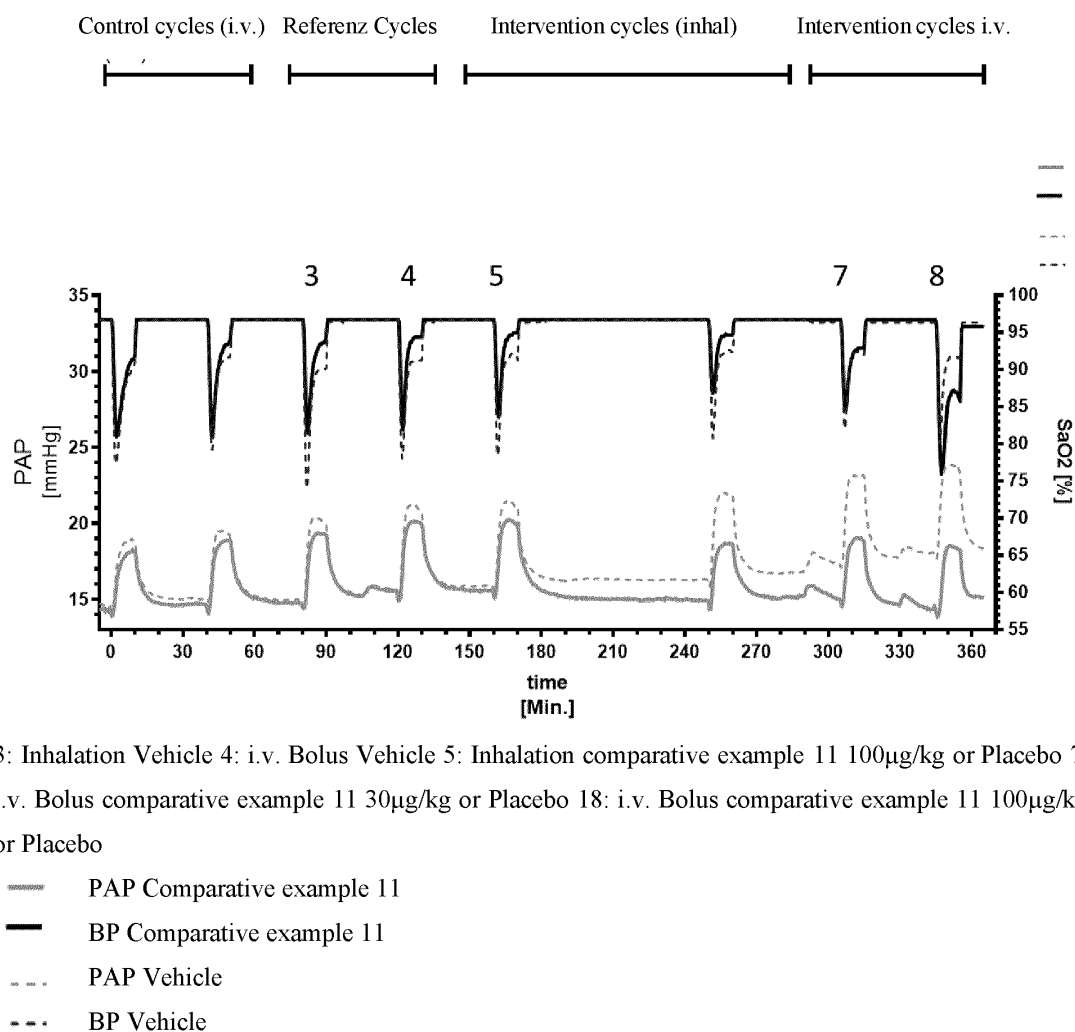


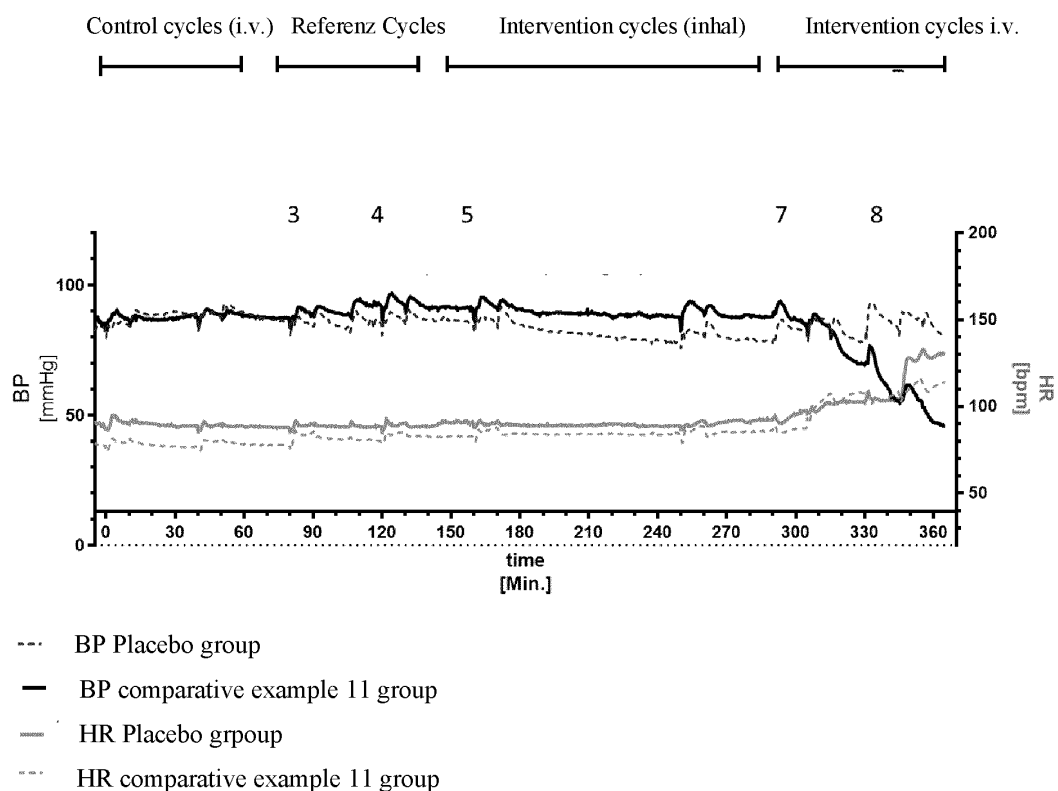
Fig. 62: Effects of comparative example 11 and comparative example 4 (100 µg/kg nominal dose) after inhaled application 1, 5, 12, 16 and 24 hours before hypoxia on decrease in PAP during hypoxia in conscious dogs. Data are shown as mean ± SEM (n=3)



3: Inhalation Vehicle 4: i.v. Bolus Vehicle 5: Inhalation comparative example 11 100µg/kg or Placebo 7: i.v. Bolus comparative example 11 30µg/kg or Placebo 8: i.v. Bolus comparative example 11 100µg/kg or Placebo

Fig. 63: Effects of comparative example 11 after inhaled and i.v. application and of vehicle administration on PAP and SaO₂ during 8 broncho-occlusion cycles in minipigs. Data are mean (n=3-4); i.v. / iv.: intravenous; inhal: inhalation; PAP: pulmonary artery pressure; SaO₂: arterial oxygen saturation of hemoglobin

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3: Inhalation Vehicle 4: i.v. Bolus Vehicle 5: Inhalation comparative example 11 100µg/kg or Placebo 7: i.v. Bolus comparative example 11 30µg/kg or Placebo 18: i.v. Bolus comparative example 11 100µg/kg or Placebo

Fig. 64: Effects of comparative example 11 after inhaled and i.v. application and of vehicle administration on BP and HR during 8 broncho-occlusion cycles in minipigs. Data are mean (n=3-4) BP: arterial blood pressure; HR: heart rate; i.v.: intravenous; inhal: inhalation; iv.: intravenous

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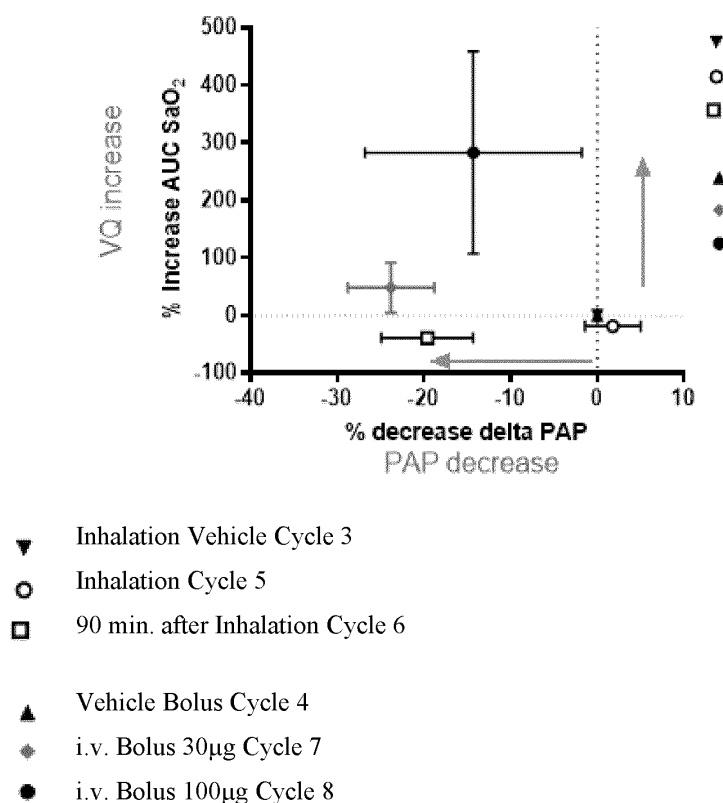


Fig. 65: Comparative example 11 capacity to decrease maximal hypoxic PAP (positive treatment effect) and AUCSaO₂ (unwanted desaturation effect) based on effects of representative cycles (n = 4 animals); data are mean ± SEM (n=4) comparative example 11 inhaled (100 µg/kg nominal dose); i.v. 30 and 100 µg/kg; AUCSaO₂: area under the SaO₂ curve; iv / i.v. : intravenous; PAP: pulmonary artery pressure; SaO₂: arterial oxygen saturation of hemoglobin; SEM: standard error of the mean; VQ: ventilation perfusion; some error bars are too small to be visible.

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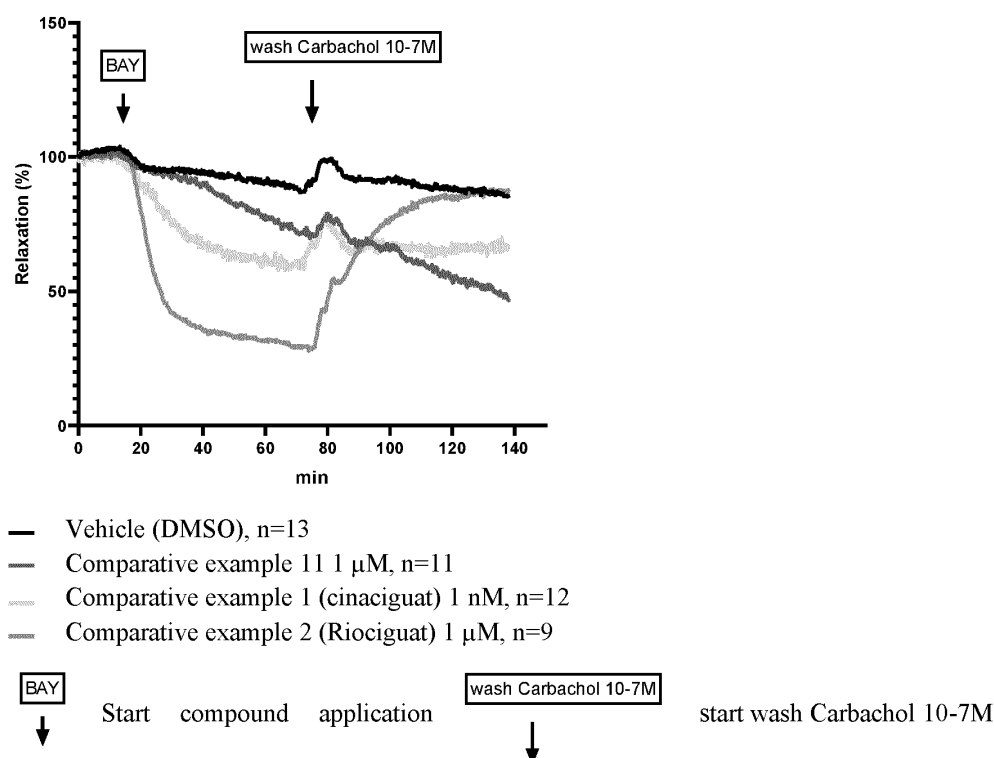
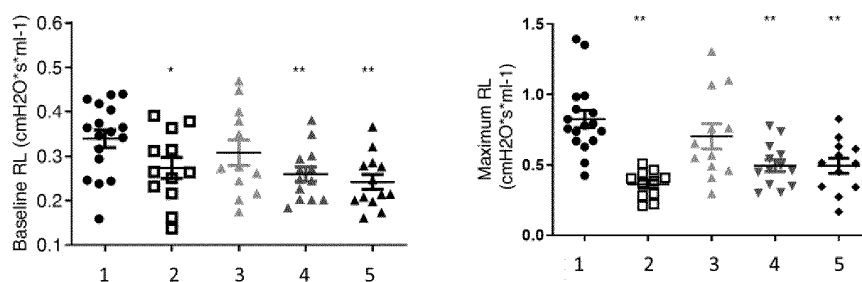
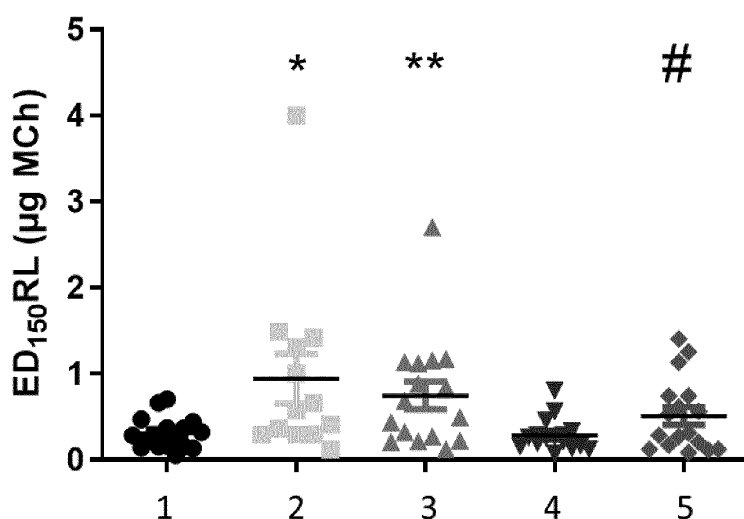


Fig. 66: Effect of comparative example 1 (Cinaciguat), comparative example 11 and comparative example 2 (Riociguat) on guinea pig trachea pre-contracted with carbachol (0.1 μ mol/L) (n = 9-13 animals); Incubation substance 1h followed by 1h wash out; data are mean values.



1: Control; 2: Tiotropium; 3: Comparative example 11 (~1 μ g); 4: Comparative example 11 (~10 μ g); 5: Comparative example 11 (~100 μ g)

Fig. 67a and 67b: Effects of Tiotropium and comparative example 11 (1, 10 and 100 μ g) on lung resistance (RL) under baseline conditions (baseline RL) and after acetylcholine challenge (Maximum RL). Data are presented as absolute values of single animals.



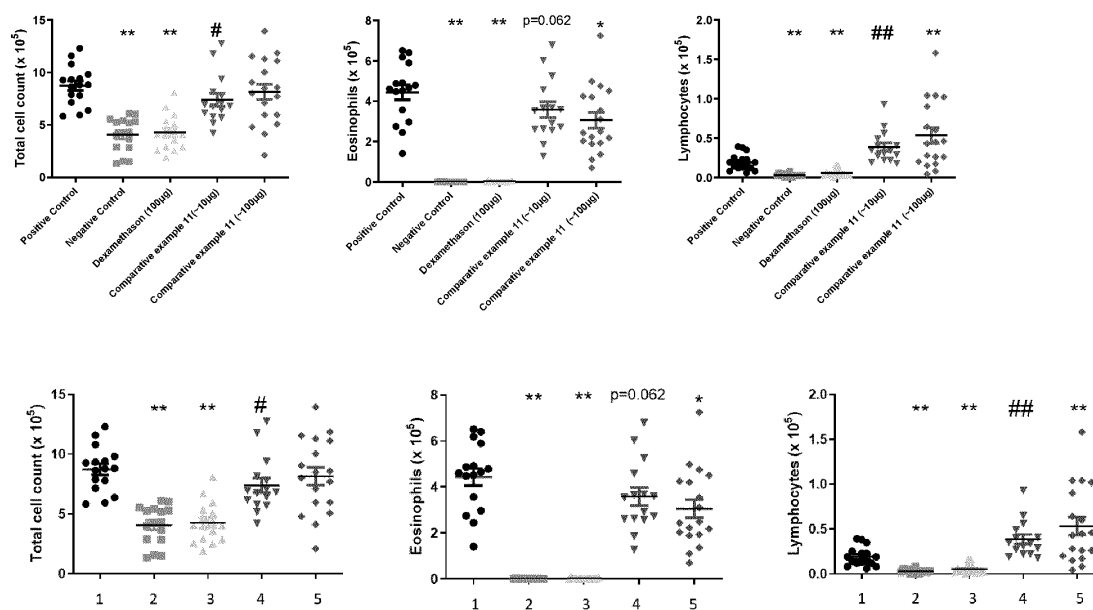
1: Positive Control; 2: Negative Control; 3: Dexamethason (100 µg) 4: Comparative example 11 (~10µg); 5: Comparative example 11 (~100µg)

Fig. 68: Airway hyperresponsiveness in the late allergic phase (24 h after final Ova challenge): Effective inhalational MCh dose (µg) to produce a 150% increase in resistance (ED₁₅₀, individual data and mean)

*p < 0.05. **p < 0.01 compared to positive control group. #p < 0.05 in single t-test)

ED₁₅₀: 150% of the maximum effective dose; MCh: methacholine; R_L: lung resistance

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1: Positive Control; 2: Negative Control; 3: Dexamethason (100 µg) 4: Comparative example 11 (~10µg);
5: Comparative example 11 (~100µg)

Fig. 69a-c: Total cell counts, number of eosinophils and number of lymphocytes in the BAL fluid 25 h after ovalbumin challenge ($\times 10^5$ /animal; individual data and means) **p < 0.01 vs. positive control group; #p < 0.05 ##p < 0.01 single t-test
BAL: bronchoalveolar lavage; vs. Versus

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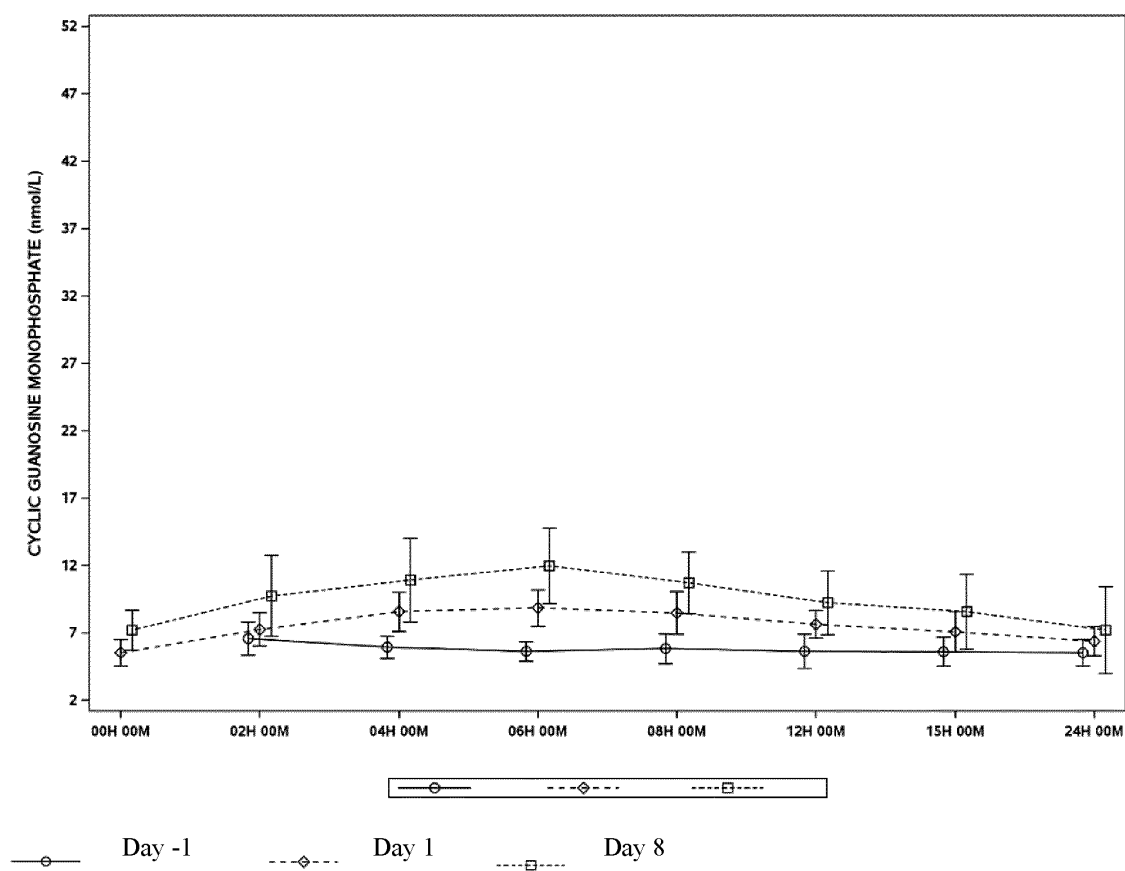


Fig. 70: Means $\pm$ SDs for cGMP (nmol/L) – comparison of pretreatment (day -1), first (day 1) and last (day 8) treatment days for the 480 μ g (example 2) dose group (SAF, N = 9)

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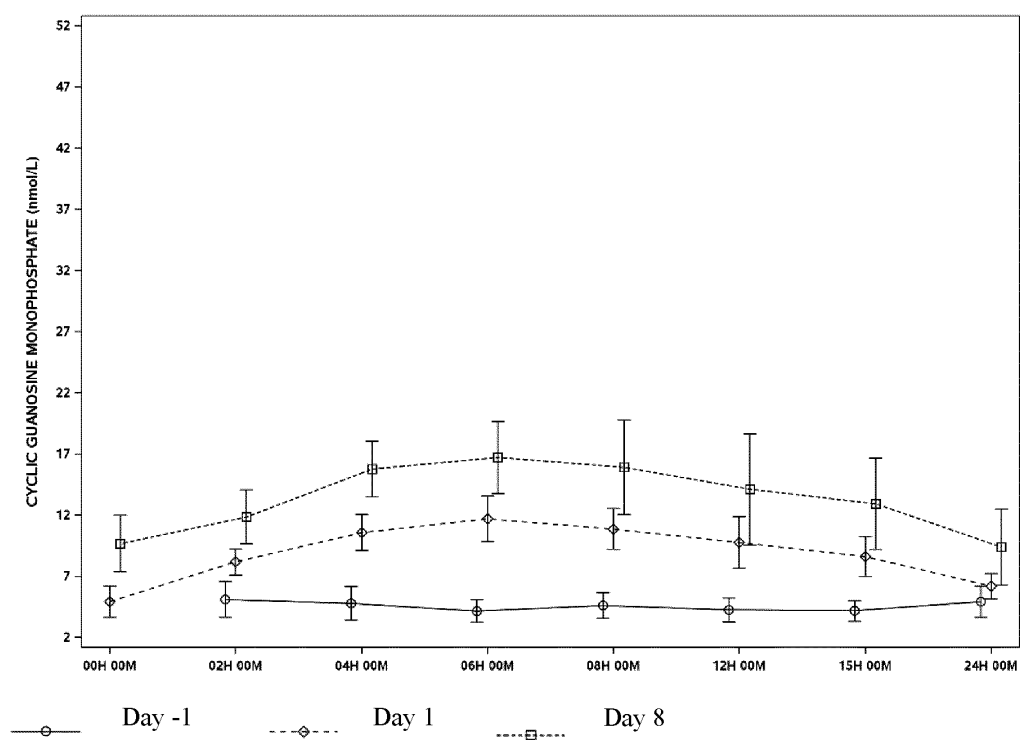


Fig. 71: Means $\pm$ SDs for cGMP (nmol/L) – comparison of pretreatment (day-1), first (day 1) and last (day 8) treatment days for the 1000 μ g (example 2) dose group (SAF, N = 9)

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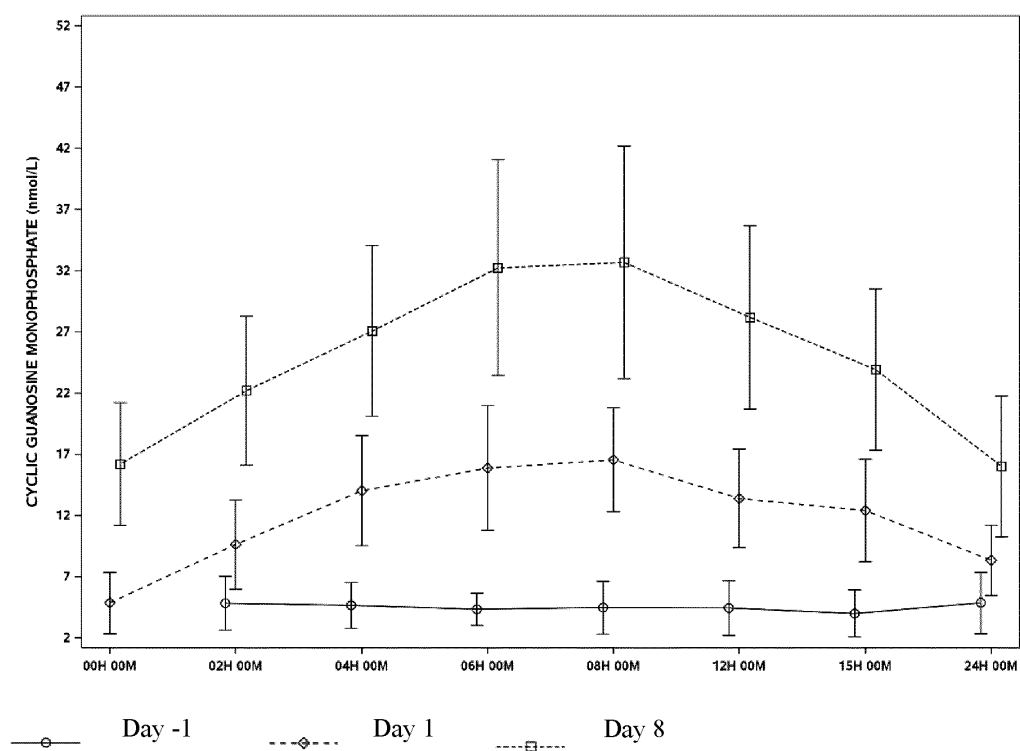


Fig. 72: Means $\pm$ SDs for cGMP (nmol/L) – comparison of pretreatment (day-1), first (day 1) and last (day 8) treatment days for the 2000 μ g (example 2) dose group (SAF, N = 9)

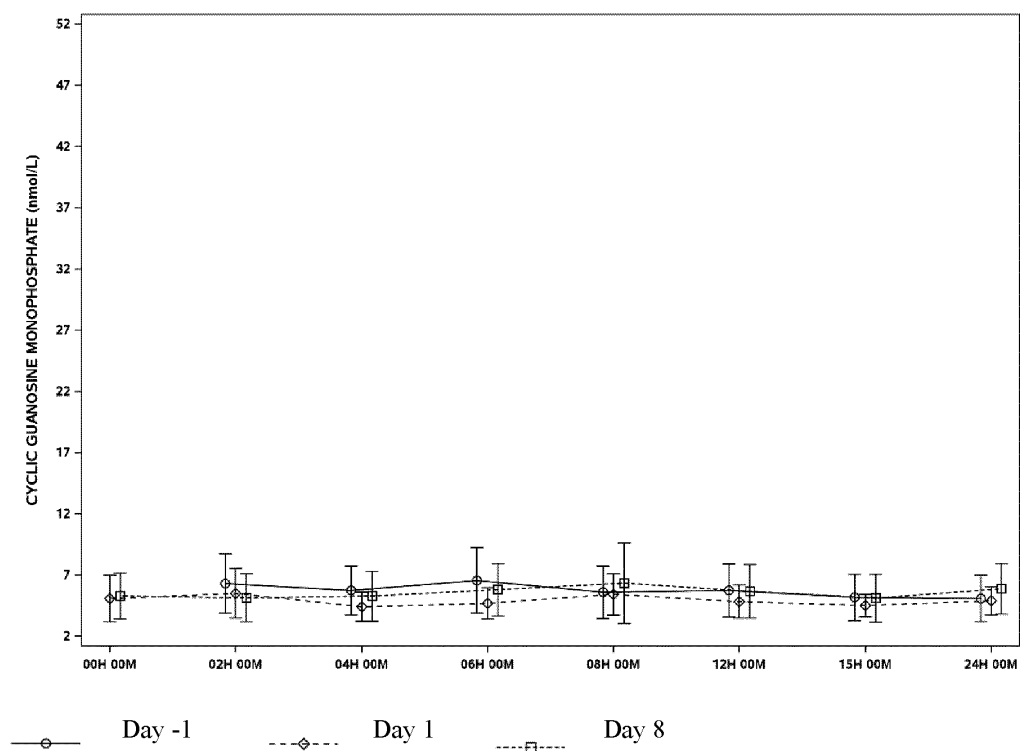


Fig. 73: Means $\pm$ SDs for cGMP (nmol/L) – comparison of treatment days for the placebo group (SAF, N = 9)

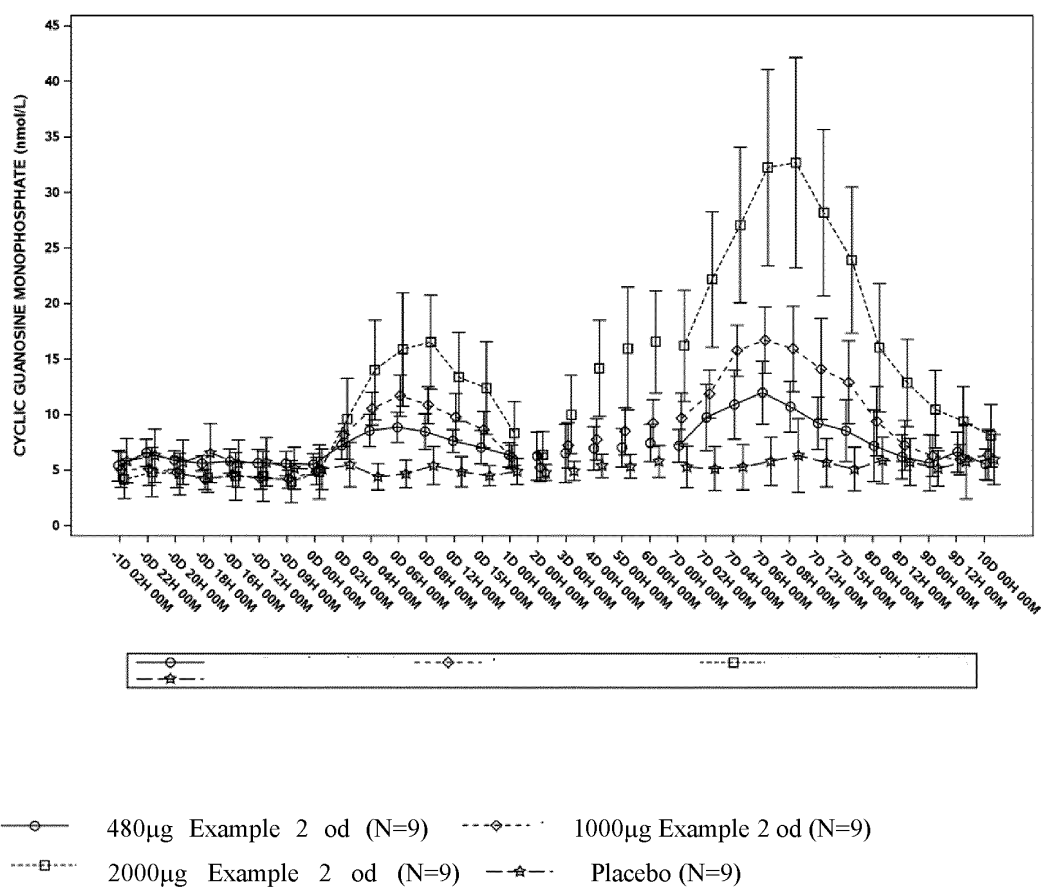


Fig. 74: Means (N = 9) $\pm$ SDs for cGMP in body liquids over time (nmol/L) on baseline day (-1d02h – 0d00h) first inhalation day (0d00h - 2d00h), trough measurements 2d00h- 7d00h) and after 7 days inhalation (7d00h- 10d00h).

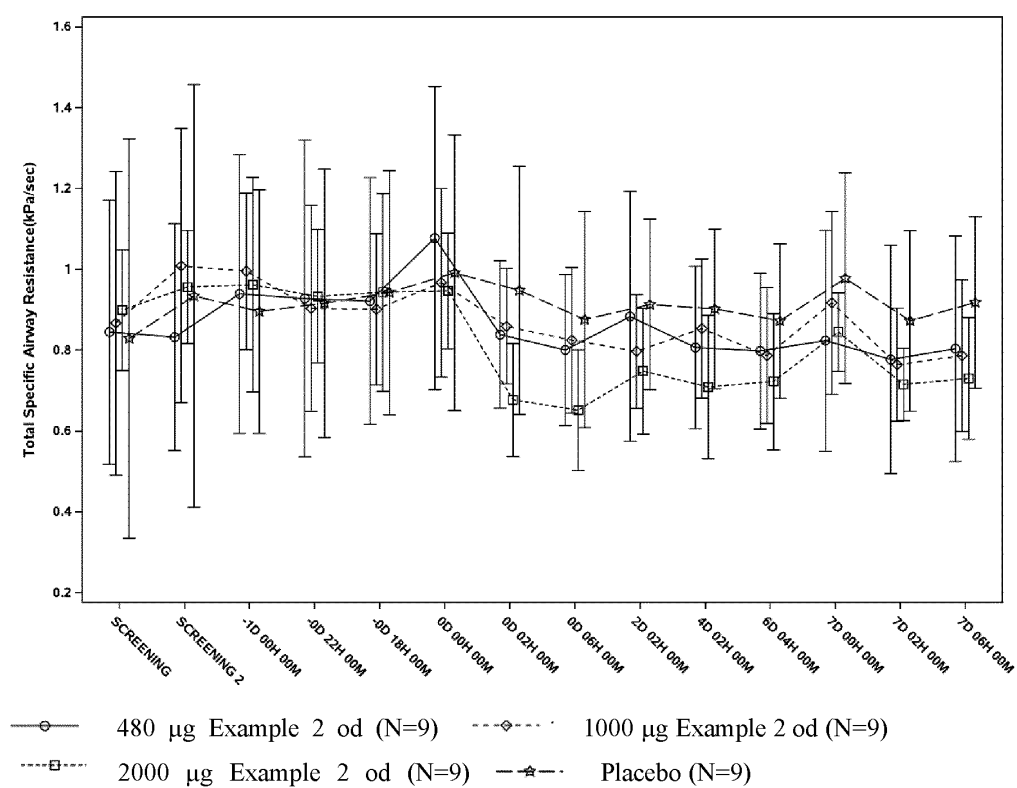


Fig. 75: Means (N = 36, 12 each for 480, 1000 and 2000 µg, example 2) and SDs for total specific airway resistance (kPa/sec) over time: screening 1/2, baseline day (-1d00h – 0d00h) first inhalation day (0d00h – 0d06h), measurements after inhalations 2d02h- 6d04h) and after 7 days inhalation (7d00h- 7d06h).

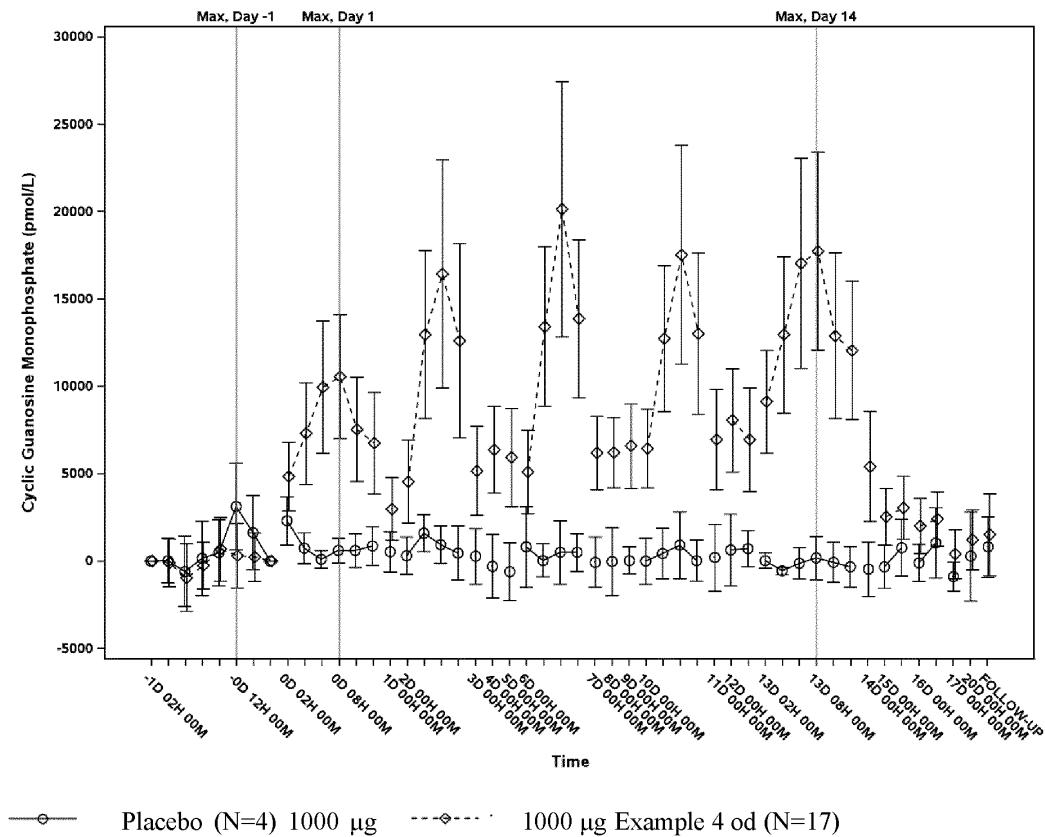


Fig. 76: Means for cGMP difference to baseline for Placebo (N = 4) and 1000 µg, (N = 17) example 4) over time (nmol/L) on pretreatment day (-1d00h – -0d09h) first inhalation day (-0d02h - 1d00h), measurements prior and after inhalations 2d00h- 2d12h, 6d00h- 6d12h, 10d00h- 10d12h) (profile days), at trough prior inhalation on days 3d – 5d, 7d-9d, 11d-12d) and for last of 14 days inhalation (12d22h- 20d00h).

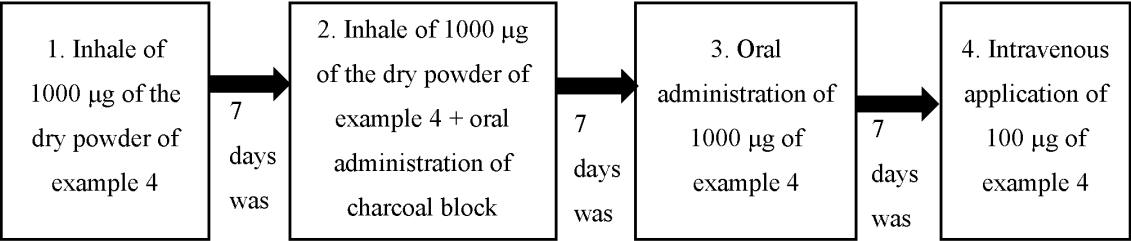
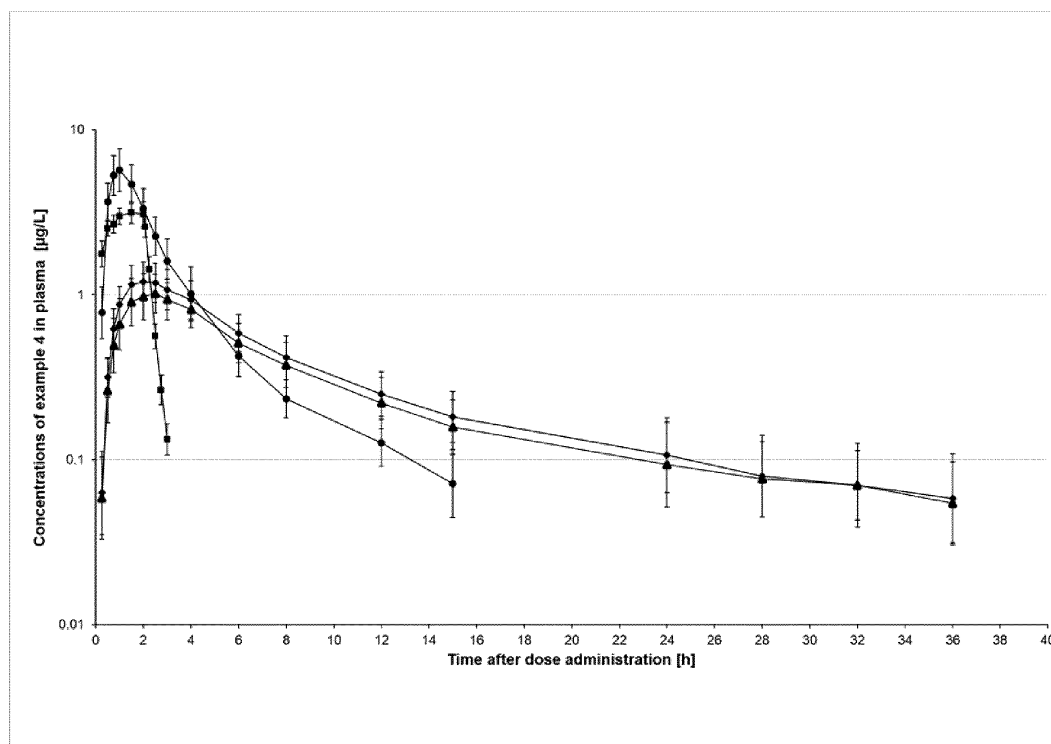


Fig. 77: scheme of the treatments conducted to investigate lung deposition



■ 100 µg Example 4 intravenous, n=15, ◆ 1000 µg inhale of example 4, n=16
▲ 1000 µg inhale of example 4 + charcoal, n=16, ● 1000 µg oral dose of example 4, n=16

Fig. 78: Geometric means and standard deviations for concentrations of example 4 (µg/L) in plasma, on semilogarithmic scale.

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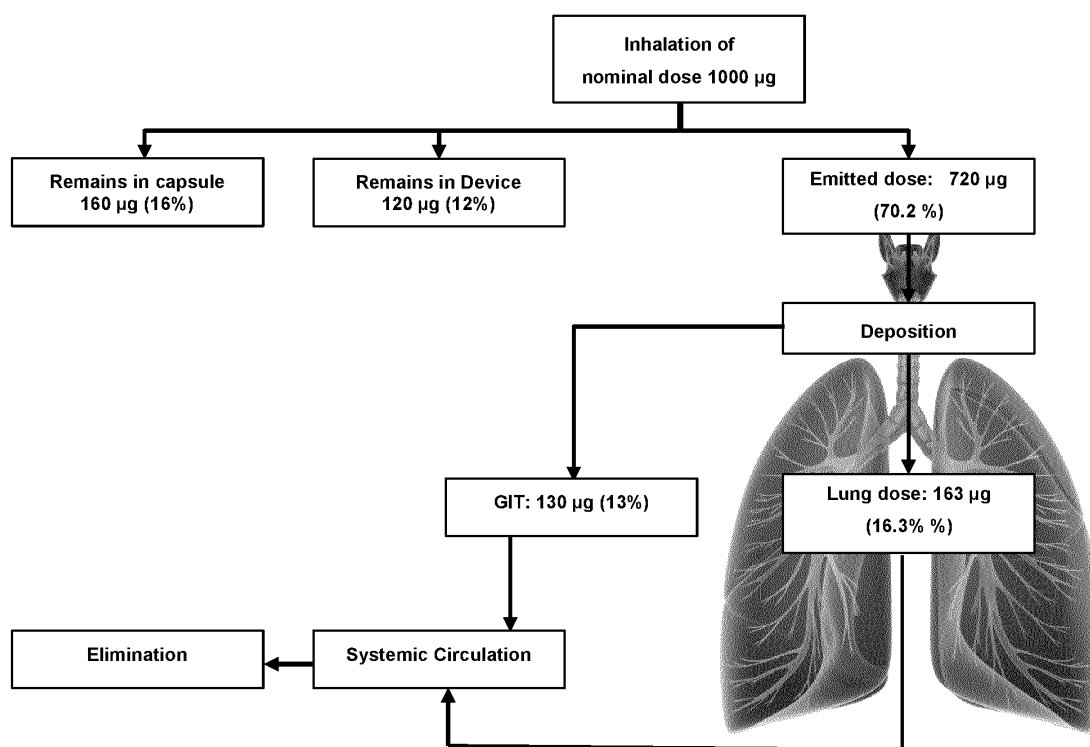


Fig. 79: Part of the dose reached the mouthpiece (emitted dose) and parts of the dose remains in the capsule, in the device, the deposited lung dose and part of the dose reached the GIT tract

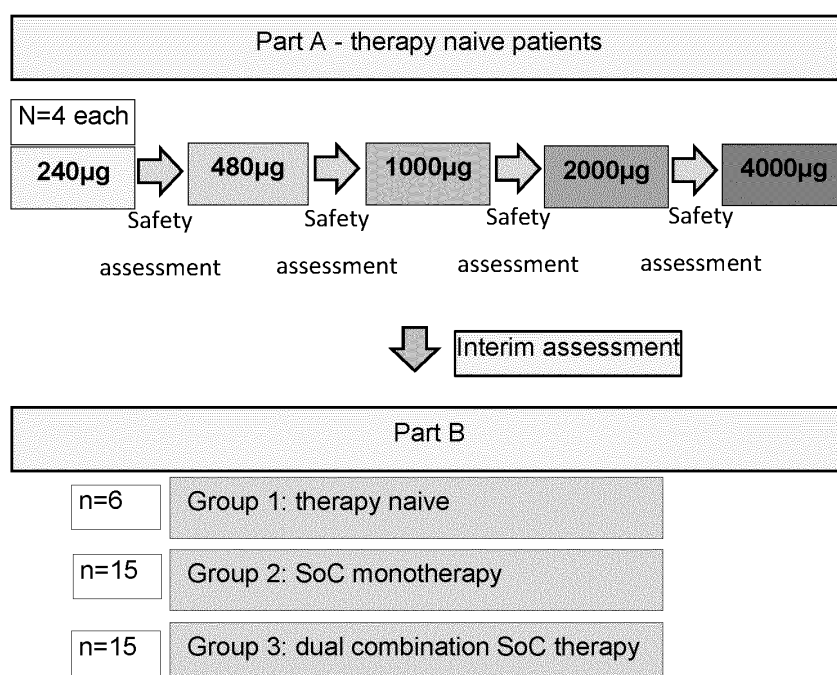
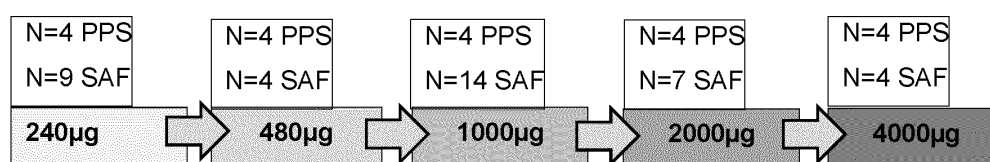


Fig. 80: study design of clinical study in patients with PAH or CTEPH



*SAF: safety analysis set: all patients matching in- and exclusion criteria (IC/EC)

*PPS: per protocol set: IC/EC met + PVR > 400 dyn + PAP decrease during inhaled nitric oxide (NO) challenge < 10 mmHG (exclusion of vasoresponsiveness)

Fig. 81: summary of conducted Part A of clinical study in patients with PAH or CTEPH

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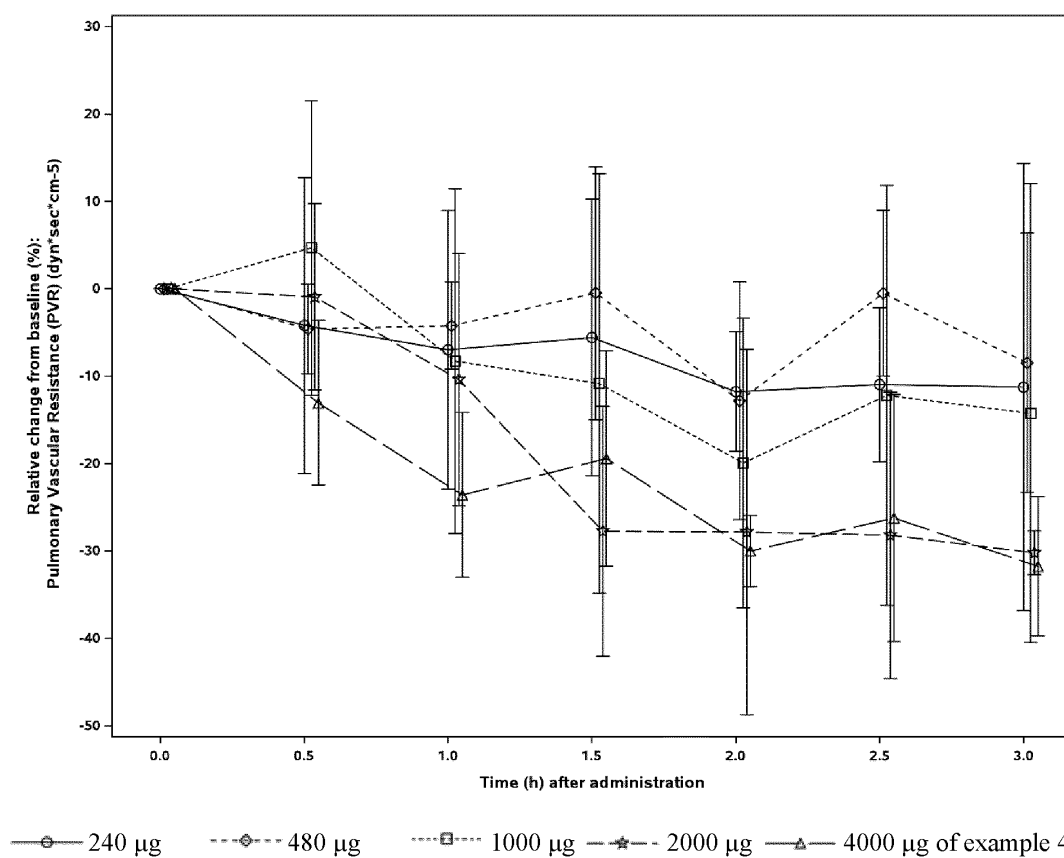


Fig. 82: Means and SDs for relative changes (%) from baseline (0D00H00M) of pulmonary vascular resistance (PVR) over time after inhalation (0D00H30M until 0D03H00M) of example 4 in patients with PAH or CTEPH (N=4 each for 240, 480, 1000, 2000 and 4000 µg group, per protocol set)

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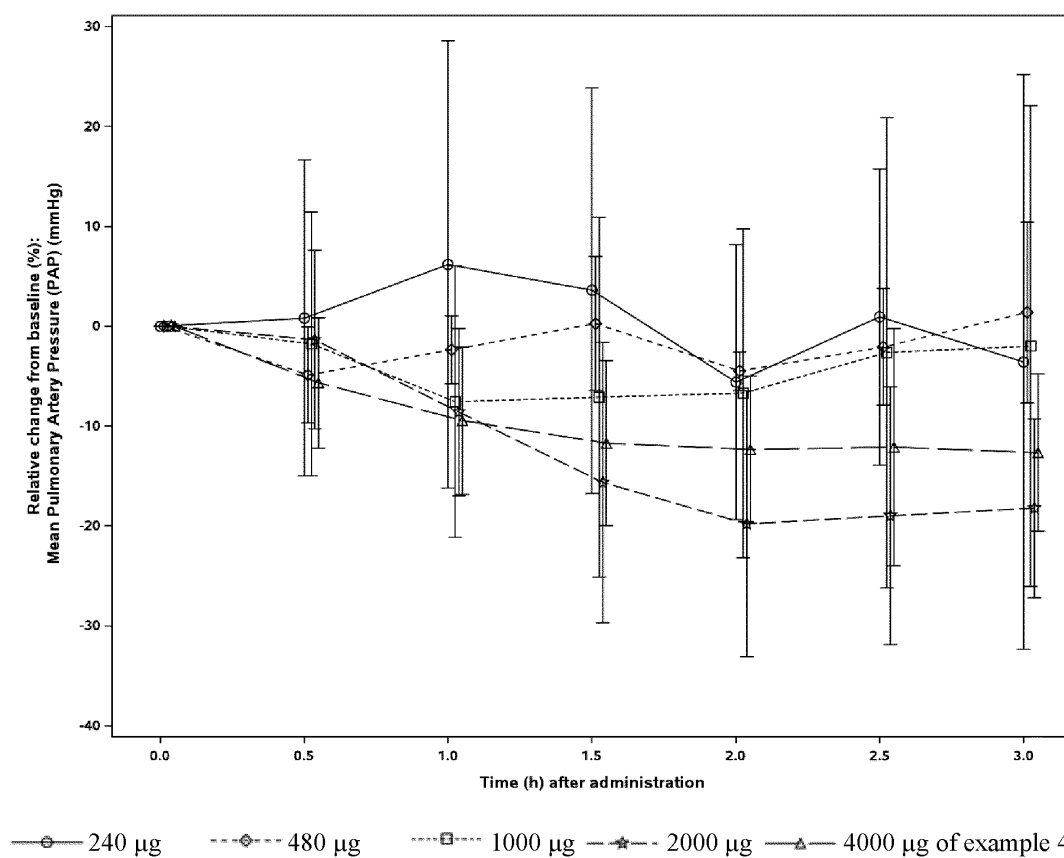


Fig. 83: Means and SDs for relative changes (%) from baseline (0D00H00M) of mean pulmonary arterial pressure (mPAP) over time after inhalation (0D00H30M until 0D03H00M) of example 4 in patients with PAH or CTEPH (N=4 each for 240, 480, 1000, 2000 and 4000 µg group, per protocol set).